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# TROPICAL DISEASES BULLETIN

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

# TROPICAL DISEASES BULLETIN.

Vol. 43.] 1946. [No. 7.

## THE TREATMENT OF AMOEBIASIS.

A Review.

By A. R. D. Adams, M.D., Ch.B., M.R.C.P., D.T.M.

### *Emetine.*

The specific treatment of amoebic dysentery dates back some three centuries, when ipecacuanha was introduced to Europe from South America as a remedy for dysentery. The employment of the drug was at first entirely empirical, and it was not until 1912 that Rogers [this *Bulletin*, 1912, v. 1, 176] showed that the alkaloid emetine exerts a potent action on *Entamoeba histolytica*, which had been recognized by Schaudinn in 1903 as the causative parasite of amoebic dysentery. The treatment of amoebiasis was thereafter established on a more rational basis, and emetine, in one form or another, has since been recognized as an essential component of any course of treatment for the acute clinical manifestations of *E. histolytica* infections.

From the time of these early experiments it has been known that emetine alone will not cure, that is completely eradicate, more than a relatively small proportion of *E. histolytica* infections of the large intestine. What this proportion is has been the subject of some discussion ; it is generally agreed to be not more than one-third of those so treated (Craig, " Amoebiasis and Amoebic Dysentery," 1934 (London : Baillière, Tindall & Cox, p. 276) puts the figure at between 10 and 15 per cent.), but there is room for a more precise evaluation of the drug as a curative agent if given in full dosage during primary clinical attacks of amoebic dysentery. The view is now widely held that the use of injections of emetine in intestinal amoebiasis should be confined to the arrest of acute manifestations, and that, when these have been controlled, the emetine injections should be stopped ; it is considered pointless to continue them indefinitely, or until a specified number have been given as a routine. One injection each day for 4 or 5 days will usually achieve the desired result, and 12 injections will do no more. The salt of emetine employed for intramuscular or hypodermic injection is the hydrochloride, and the dosage is 1 grain daily for an adult ; this dose may be divided, ½ gr. being given at intervals of 12 hours, but there is no obvious material advantage in this procedure. A patient receiving emetine injections should be confined to bed. Gross toxic effects are rarely seen from the use of the drug in normal dosage, if it is not continued for more than 10–12 days. The toxic manifestations to be watched for in practice are a rising pulse rate, irregularity in the heart's action, and a fall in blood pressure ; if these develop the drug must be stopped. Peripheral

neuritis, with wrist- and foot-drop, and even death, may occur, but these are rarely encountered except when the dosage has been injudicious and the course unduly prolonged. Emetine should never be given intravenously.

### *Metastatic Infections.*

In addition to their rapid action in controlling acute clinical exacerbations of amoebiasis due to primary infection in the gut, emetine hydrochloride injections act specifically in arresting, and in most cases in eradicating, secondary amoebic infections in other organs and tissues, provided that treatment is not unduly delayed. In liver infections the parasites are usually destroyed by one course of a dozen daily injections of emetine hydrochloride, and this is equally true of infections of the lung, of the skin, and of those direct extensions of the infection from intestinal lesions to neighbouring organs and structures which result in the formation of amoebic granulomata (amoebomata) in the abdomen. Where such diffusions of the infection from the primary focus in the large bowel occur, a course of 12 injections of emetine, one a day, should therefore be given at once to kill the amoebae in the secondary lesions. Surgical intervention may also be necessary, but this can usually be averted if the condition has not been allowed to develop too far before the emetine is administered. It is wise to adopt a conservative attitude to surgery, and to await developments before deciding on operative interference: remarkably large amoebic liver abscesses, so long as they are bacteriologically sterile, are often absorbed when the causative parasites have been destroyed by emetine treatment. Where evacuation of an amoebic liver abscess is deemed necessary, open drainage of the cavity is now generally held to be preferable to aspiration; the latter usually has to be repeated, and often proves inadequate, so delaying the more radical procedure. In no case where surgery is resorted to must the fundamental sterilization of the lesion by parenteral emetine injections be overlooked, or the erosive process will continue and the parasitic infection will extend into the tissues involved in the operation. There is no point in putting emetine into the abscess cavity, where it acts as a local irritant and does not appear to reach the tissues infiltrated with parasites around the lesion.

Where such secondary infections with *E. histolytica* occur, it must never be forgotten that the primary infection is in the large intestine, and that the successful treatment of the secondary lesion leaves this primary infection, in most cases, unaffected.

### *Treatment of the Intestinal Infection.*

The eradication of an *E. histolytica* intestinal infection, whether the patient be harbouring a symptomless infection, and passing formed stools containing the cystic form of the parasite, or be suffering from recurring frank amoebic dysenteric attacks with the passage of blood and mucus, containing the vegetative stage of the parasite, is, in general, easy of achievement. A number of drugs administered by the mouth, or in the form of colonic retention enemata, are employed for the purpose, although none of these can be claimed as entirely specific, in that each given alone fails to cure a considerable proportion of cases. It is a common practice, in view of this, to use several drugs concurrently, or in sequence, in the belief that their combined action is greater than that of any single one of the series, and the "combined treatments" of various authors [this *Bulletin*, 1945, v. 42, 559, 731, 895 and 999] are the result. These treatments, broadly, have much in common; and in most cases of latent amoebiasis, and of early previously untreated relapsing amoebic dysentery, are all effective in eradicating the infections. There seems to be no substantial evidence that any one of the courses is greatly superior to the others, provided that the

drugs are given so that they are liberated and retained for an adequate time in the correct part of the gut. MANSON-BAHR [this *Bulletin*, 1945, v. 42, 207] directs attention to the importance of the selection of drugs in a suitable form, and of their proper administration in order to obtain satisfactory results. The drugs usually employed consist of an emetine preparation for oral administration (emetine-bismuth-iodide, Auremetine), a trivalent arsenical similarly given (Stovarsol, Carbarsone), and one of the iodo-oxy-quinoline series (Diodoquin, Enterovioform, Chiniofon) for oral use or as a colonic retention enema.

Toxic complications sometimes result from the administration of the arsenicals to susceptible individuals, which usually at first take the form of skin eruptions, and reduction in the dosage or withdrawal of the drug will arrest the trouble; if the drugs are continued, grosser manifestation of arsenical poisoning may occur. Very occasional deaths have been recorded from the employment of the arsenicals, and even of Carbarsone, which is usually regarded as the least toxic of them [MAYER, *Lancet*, 1946, April 27th, 631].

For the treatment of a symptomless carrier of the infection the procedure would consist of the administration of one of the "combined courses" referred to above. For the treatment of an early uncomplicated and previously untreated case of relapsing amoebic dysentery, seen during an acute exacerbation of the disease, the procedure would be the administration of emetine injections for three or four consecutive days to arrest the clinical attack, immediately followed by a "combined course" to eradicate the infection. In a case of amoebiasis complicated by a secondary lesion, such as early embolic infection of the liver, twelve daily injections of emetine would be given to sterilize the liver lesions, and a "combined course" of treatment to sterilize the gut infection would follow immediately. If drainage of the liver lesion proved necessary, the "combined treatment" of the intestinal infection might well be delayed, after completion of the emetine injection course, until the patient was convalescent from the operation, but there should be no undue waste of time in tackling the intestinal focus.

### *Criterion of Cure.*

The criterion of cure of an intestinal *E. histolytica* infection is the continued complete absence of parasites from the stools after treatment. For a week or two after unsuccessful intensive treatment, parasites will probably be too few in number in the stools to be found microscopically. Stool examinations should, therefore, be deferred for a couple of weeks after conclusion of the treatment and at least a dozen specimens, taken on consecutive days, should then be searched for parasites. If this search is competently made, and no *E. histolytica* is found, the presumption of cure is considerable, though not absolute. Certain cases of persistent infection may escape notice, and where possible, in order not to miss these, serial stools should subsequently be examined at intervals over a period of at least twelve months.

### *Refractory Cases.*

During recent years a considerable number of men were invalided from the various war fronts in the East, with severe relapsing amoebic dysentery which had yielded only temporarily to the treatments available under fighting conditions. Many of these men had received very large numbers (100 or more) of injections of emetine hydrochloride, and some had, in addition, been treated with the arsenical or iodo-oxy-quinoline series of drugs. Some of these cases proved refractory to any of the "combined courses" of treatment referred to above, even after repetition on several occasions; although they temporarily

benefited from them in that the clinical manifestations of their dysentery abated, the intestinal infection was not cured, and clinical exacerbations of dysentery recurred, usually in severe form, within a few days or a week or two of completion of the course. Such cases, it is held by some workers, had developed resistance to emetine as a result of the undue amount of this drug given them while in the field ; but while there is some clinical evidence that emetine-resistance may occur in individual cases of amoebic dysentery, the development of emetine-fastness in a strain of *E. histolytica* has not yet been conclusively demonstrated *in vivo* or *in vitro*, and its existence is still subject to proof. Nevertheless, it is probably sound policy to assume that it may occur, and to forestall it by avoiding prodigal and needless resort to emetine injections in the treatment of amoebic dysentery.

### *Associated Bacterial Infection of the Bowel Wall.*

Another explanation of the difficulty experienced in sterilizing some chronic relapsing amoebic dysenterics of their parasites is the establishment of an extensive concurrent bacterial infection of the tissues of the gut wall. On microscopical examination of the stools of such individuals, pus will usually be found, and on sigmoidoscopy, ulceration and a generalized inflammatory condition of the mucosa may be seen. A secondary bacterial colitis is coincident with the primary amoebiasis, and this concomitant bacterial colitis probably renders the amoebic dysenteric infection more difficult to eradicate. The colitis not infrequently persists, as a chronic post-dysenteric colitis, after the successful eradication of the amoebic infection. That its presence makes the amoebiasis more resistant to treatment is to some extent substantiated by the experience of certain workers, who, either prior to, or concurrently with, a combined course of treatment for the intestinal amoebiasis, now give a therapeutic course of one of the sulphonamide drugs (sulphaguanidine, succinyl sulphathiazole or phthalyl sulphathiazole) or of penicillin in massive dosage, or of both, with improvement in the cure-rates for the amoebiasis in such cases. When a patient has proved refractory to previous treatment, or has suffered for long from an untreated relapsing amoebiasis, or when pus is found in the stools or there is sigmoidoscopic evidence of a diffuse inflammatory or ulcerative condition of the large bowel, such preliminary treatment with a sulphonamide drug or penicillin, or both, is advisable. HARGREAVES [this *Bulletin*, 1945, v. 42, 559, 895] has claimed very good results with an initial dose of 100,000 units of penicillin intramuscularly, followed by 33,000 units every 3 hours, to a total of one or two million units, and succinyl sulphathiazole to a total of 80 gm. by the mouth. The writer's practice is to give succinyl or phthalyl sulphathiazole and Chiniofon, each by the mouth, on alternate days for ten days prior to " combined " therapy in such cases ; and he has not found penicillin so generally effective as has Hargreaves in relieving or arresting a severe bacillary colitis. It is to be clearly understood that the sulphonamides and penicillin have no direct action on the amoebae ; their action is exerted on the secondary bacterial invaders. Nevertheless, evidence accumulates that control of a gross secondary bacterial invasion of the wall of the large intestine leads to more effective action of any treatment directed against the *E. histolytica* infection.

### *Diet and Management.*

There is general agreement also that a liberal, nutritious, easily assimilable and palatable diet is of benefit in these cases, and that adjuvants in the form of vitamin concentrates may play a part in promoting bodily resistance. Whether confinement to bed throughout " combined " treatment is necessary or desirable must be determined by the circumstances of each individual case.

Complicating infections should be dealt with and the general condition be maintained at as high a level as possible. Abstinence from the bulkier alcoholic drinks is advisable, and the maintenance of the morale of patients suffering from such a disease is an important factor in their successful treatment, as willing co-operation is of fundamental importance to its achievement.

Finally, when the amoebiasis has been successfully eradicated, any troublesome sequelae, such as the haemorrhoids commonly found in association with a diarrhoeic disorder, must receive attention before the patient is discharged as cured.

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## SUMMARY OF RECENT ABSTRACTS.*

### VI. PLAGUE.

*Epidemiology: Transmission.*

In *Public Health Reports* (p. 32) is a record of the only human case of plague notified in the United States during 1943. This case, in a child aged two, was unusual in that death took place two months after onset, and was due to bubonic plague with chronic plague encephalitis. Plague is widespread in rodents in the United States.

In the *Epidemiological Information Bulletin* of the Health Division of UNRRA (p. 724) there is an account of an outbreak of plague in Western Yunnan, near the Burma frontier, where plague has long been endemic. Most of the patients had received one or more inoculations of vaccine, but though this had not been enough to prevent infection, the death rate in the vaccinated was much lower than in the non-vaccinated [see also MUNTER below]. Sulphadiazine, in a small series of cases, appeared to give better therapeutic results than sulphathiazole or serum.

SHIH and POLLITZER (p. 725) have calculated the point at which the incidence of plague in the rat population of central China becomes a serious threat to man. They have found that the situation is reassuring so long as the incidence of infected rats is well below 20 per cent., but human plague is imminent if a level of 25 per cent. is reached.

POLLITZER and LI (p. 726) discuss the decline of epidemics of pneumonic plague in China. The principal factor seems to be the diminishing incidence of cases with cough and bloody sputum, teeming with bacilli. The danger of infection from patients with plague pneumonia but without bloody sputum is much less than from those with the classical signs.

LE GALL (p. 280) contributes an account of plague in Madagascar, making the point that the incidence rose to a high level about 1932, and fell rapidly after the institution of vaccination, on a large scale, with the live E.V. vaccine. Pneumonic plague is common in the high plateau region, and is a respiratory disease of direct transmission. For bubonic plague, *X. cheopis* is the usual vector, and this flea can live for some time away from rats; for this reason the rat flea index is not now regarded as important in epidemiological studies. Continued examination of captured rats, for plague infection, seems now to be superfluous in Madagascar. Treatment with E.V. anti-plague serum and sulphonamides gives good results in bubonic plague, but not in the pneumonic infection.

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* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

BLANC and BALTAZARD (p. 33) quote an experiment which, in their view, tends to discredit the theory that blocking of infected fleas is an important factor in the transmission of plague. A group of *Xenopsylla cheopis* were infected, and remained infective during a span of life which did not differ from the normal. If transmission is a function of blocking, and if, as is usually supposed, a blocked flea does not live long, it would appear that the fleas became blocked successively, which is unlikely. The authors think, rather, that the principal factor in transmission is the multiplication of bacilli in fresh blood taken up in frequent feeds ; an infected flea, after a fast of 15 days, is unable to infect by its first bite, but becomes infective less than 12 hours later. This view is supported by experiments on other arthropods in which blocking does not occur. It has a bearing on human plague, since *X. cheopis* attacks man only when urged by hunger. The same authors [this *Bulletin*, 1944, v. 41, 281] maintain that, in Morocco, transmission of plague from man to man by *Pulex irritans* is by no means uncommon. GIRARD (p. 375) discusses this question, and concludes that although the prevalence of *P. irritans* may create special infective conditions in Morocco, the really important vector in general is *X. cheopis*. He upholds the view that blockage of the proventriculus, which occurs in *X. cheopis* but not in *P. irritans*, is an important factor in transmission.

Girard makes the point that *X. cheopis* may exist for long periods away from the rat (see LE GALL above), and emphasizes the overriding importance of eliminating contact between rat and man, in the control of plague. In replying to Girard, BLANC and BALTAZARD (p. 376) uphold the two propositions that the human flea and louse usually become infected on man in the agonal period, and that they can transmit plague. They point out that *P. irritans* is strikingly averse to biting guineapigs, and that this fact has vitiated much laboratory experimental work ; it will, however, bite man freely.

HECHT (p. 281) has shown that although in part of Venezuela *Rhopalopsyllus* is usually the most common flea on trapped rodents, there is from time to time a considerable increase in the proportions of *X. cheopis* and *X. brasiliensis* caught.

JELLISON (p. 805) records the host relationships and geographical distribution of fleas of the genus *Oropsylla* in North America.

In a survey of sylvatic plague in part of Argentine, SAVINO and KUSNETZ GOOBAR (pp. 33, 466) found natural infection in *Graomys griseoflavus centralis*, which is known to have contacts with human habitations, and in several cats.

SAVINO *et al.* (p. 558) describe a chronic encapsulated abscess, containing living plague bacilli, in the spleen of a rat. This is a very rare condition, and may indicate the means by which infection is carried over from one plague season to the next.

### *Aetiology.*

MACCHIAVELLO and URIGUEN (p. 466) think that although invasive capacity and toxicity of *P. pestis* are to some extent interdependent, they may differ quantitatively. Strains from the Andean region of Ecuador are highly invasive, belong to the S and not to the R form, are of relatively low toxicity, and are peculiarly pneumotropic. It seems that the very mildness of plague in that region allows time for the production of secondary pneumonic plague, to a greater extent than elsewhere.

DEVIGNAT (p. 806) reports a sudden chromogenic dissociation, perhaps even a mutation, giving colonies of typical R and S type, with yellowish coloration, in the E.V. strain of the 104th passage.

WOODWARD (p. 281) has shown that *P. pestis* has an action in decomposing the ribonucleic acid of yeast.

### *Treatment.*

A case of laboratory infection with plague is reported from San Francisco (p. 33) [this is presumably the case referred to by MUNTER, below].

Recovery from primary pneumonic plague is very rare. MUNTER (p. 805) reports the case of a doctor in the United States, who was engaged on plague investigation and who, about one year before he contracted plague pneumonia, had received five injections of plague vaccine. The diagnosis of plague pneumonia was completely established, and treatment with sulphadiazine was instituted at an early stage; the patient recovered, and the very careful precautions taken to prevent spread of the disease to those who attended him were entirely successful. The author makes the point that recovery cannot be attributed solely to the action of the drug, since other factors, *e.g.* the vaccination, may have contributed to the favourable result [see the UNRRA report, above].

In an alternate-case trial of sulphadiazine and sulphathiazole in plague, in an adequate series of patients, WAGLE (p. 558) has shown that though each drug is valuable, sulphadiazine is considerably more effective than sulphathiazole; the case mortality rates in the two series were 21·9 and 33·7 per cent. respectively when no differentiation was made between septicaemic and non-septicaemic cases, and 12 and 21 per cent. when patients moribund on admission were excluded. The dosage for sulphadiazine was 10 gm. the first day and 6 gm. on subsequent days. DE VILLAFANE LASTRA (p. 892) treated 35 patients (four of whom had septicaemic plague) with sulphathiazole in high dosage, 10–12 gm. daily for adults, giving a blood level of over 8 mgm. per 100 cc., for not less than 6 days. There were five deaths, all in patients with bubonic plague, and in four of these, plague meningitis was present.

The case mortality rate from plague in part of Hawaii, between 1910 and 1944, was almost 100 per cent., compared with 49 and 32 per cent. in San Francisco and New Orleans. WITLIN and WILBAR (p. 642) therefore investigated the therapeutic effect of penicillin, experimentally, in Hawaii; all the guineapigs died, and the result was wholly disappointing.

MACKAY-DICK (p. 377) notes a series of severe urticarial reactions in British soldiers who received injections of anti-plague serum; none of the Indians similarly treated showed this effect.

### *Control: Vaccination.*

HUNDLEY and NASI (p. 282) recall that plague was found in Tacoma, in rats, for the first time in 1942. An intensive campaign was undertaken, and so far as can be determined, the infection was brought under complete control at a reasonable cost. The measures included trapping, poisoning, gassing, fumigation, food sanitation, harbourage elimination, rat proofing, quarantine and educational activities. SHIH *et al.* (p. 726) describe the measures taken to control plague in two small towns in China.

In an investigation into the immunizing power of living attentuated vaccines in plague, HSUE (p. 726) concludes, from animal experiments:—that dead vaccines are unsatisfactory; that attenuation of virulent bacilli can be effected by continual subculture at 41–42°C.; that a spontaneously attenuated strain had much better immunizing power than artificially attenuated strains; and that antigenic potency of living vaccines is higher the further they diffuse, into the internal organs, from the site of injection.

ABRAMOVA (p. 642) shows that vaccination with an avirulent live strain of *P. pestis* causes an increase in the opsonic index of animals, but in his experiments, correspondence between the degree of immunity, as tested by subsequent virulent inoculation, and the opsonic index, was not exact.

It has long been known that guineapigs rendered partly but not completely resistant to plague by injection of vaccine or immune serum, are especially liable to death from secondary plague pneumonia, after virulent infection. GIRARD (p. 377) raises the question whether the prevalence of pneumonic plague in Madagascar can be explained by some such mechanism, the result of the extensive use of live E.V. vaccine, and whether a state of incomplete immunity could restore the virulence of the living organisms of which the vaccine is composed. He answers these questions in the negative, showing that pulmonary complications are not more common in the vaccinated than in the unvaccinated, and that the incidence of pneumonic plague has diminished in Madagascar *pari passu* with the total incidence of all forms of plague. Man, therefore, appears to differ from the small rodents in liability to plague pneumonia after insufficient immunization. *Charles Wilcocks.*

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## MALARIA.

RUSSELL, P. F. **Lessons in Malariology from World War II. The Charles Franklin Craig Lecture, 1945.** *Amer. J. Trop. Med.* 1946. Jan., v. 26, No. 1, 5–13. [14 refs.]

BELTRÁN, E. Notas críticas sobre terminología paludológica. [**Critical Notes on the Terminology of Malaria.**] *Bol. Oficina Sanitaria Panamericana.* 1945, Oct., v. 24, No. 10, 879–92. [16 refs.]

BRIERLY, W. B. **Malaria and Socio-Economic Conditions in Mississippi.** Reprinted from *Social Forces.* 1945, May, v. 23, No. 4, 451–9, 4 graphs.

In establishing a definite relationship between socio-economic conditions and malaria mortality from year to year in the State of Mississippi, the author deals with a neglected aspect of malaria epidemiology. The prosperity of Mississippi is mainly dependent upon cotton cultivation. Cotton tenant farmers are among the poorest farmers in the United States : in many areas they live at subsistence level, their existence depending upon the price of a single commodity. The cotton-growing areas have an inadequate supply of food crops and their inhabitants live on a meagre and ill-balanced diet. There is a definite relationship between the price of cotton (retarded for one year), and net return from personal income tax, and malaria mortality in the State from year to year. During years in which income is high the people have more, and more varied, food ; their homes are kept in better repair, especially in regard to screening ; and if suffering from malaria they have money for medical services and adequate antimalarial drugs. During years of low income the reverse is the case.

About 950,000 people of the 3,100,000 population of Mississippi are in the tenant-farmer group. They have nomadic habits ; 26 per cent. of them operate the same farm for only one year, or less ; then they move on in search of a better job. Eighty per cent. of all tenant farms are occupied by farmers who have been on the farm for less than five years. This mobility accounts in some measure for the low socio-economic level.

In Mississippi, socio-economic conditions appear to explain adequately the cyclic exacerbations of malaria every five, six or more years, which have characterized the disease in the southern United States. *Norman White.*

BRIERLY, W. B. **The Influence of Surface Features upon the Distribution of Malaria in Northwestern Mississippi.** Reprinted from *J. Geography.* 1945, Nov., v. 44, No. 8, 312–24, 3 figs.

The influence of physiographic conditions in determining variations in malaria incidence is well illustrated in this study. The delta region in north-west Mississippi is a flat monotonous plain. It slopes only four or five inches to the mile southward and eastward and contains innumerable swamps and other collections of water favourable for the breeding of *Anopheles quadrimaculatus.* The Loess Bluff Upland, which borders the delta region to the east, is a rough, rolling, hilly area with relatively few hydrographic features. Malaria is much more prevalent in the delta. *Norman White.*

LE GAC, P., SEITE, P. & COMBESCOT DE MARSAGUET, G. Étude sur le paludisme à Ouagadougou. [**Study of Malaria in Wagadugu.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 7/8, 201–16, 1 fig.

A severe outbreak of malaria in Wagadugu at the close of 1941 and the beginning of 1942 prompted the malaria survey, the results of which are here recorded. (Wagadugu is the capital of Mossi in French West Africa, just north of the Gold Coast Colony.)

An examination of 2,942 children from 2 to 12 years of age during the rainy season, June to October, revealed a spleen rate of 37·15 and a parasite rate of 53·67 per cent. The corresponding rates for 808 children in 7 adjacent villages were 44·55 and 50·49 per cent. The gametocyte rates of these two groups of children were 14·81 and 22·76 per cent. *P. falciparum* was responsible for 93 per cent. of infections, the remainder being due to *P. vivax* ; *P. malariae* was not found.

Three species of *Anopheles* were found, *A. gambiae, A. funestus* and *A. nili. A. gambiae* is much the most prevalent. Marigots constitute the chief breeding places. (A marigot is a river that loses itself in the ground ; often dry in the dry season, it is subject to flood in the rains.) In Wagadugu certain of the marigots are dammed so as to contain water throughout the year. The laterite soil favours the creation of temporary breeding places suitable for *A. gambiae* breeding. Of anophelines breeding in marigots only 5 to 6 per cent. are *A. funestus*, the remainder being *A. gambiae. A. nili* breeds in wells, in which 72 per cent. of the anopheline larvae taken were of this species. In Wagadugu there are some 1,880 wells, never more than 10 to 12 metres in depth, and generally dry for two or three months in the year. Anopheline larvae were found in 452 of the 1,880 wells examined. Wells dug or drilled to a greater depth, tapping an underlying sandy stratum, are capable of supplying abundant pure water all the year round and would obviate the necessity of relying on marigots for the supply, as hitherto.

The very great scarcity of oils for use as larvicides contributed to the exceptional severity of malaria in 1941–42. *Norman White.*

RIBBANDS, C. R. **Moonlight and House-Haunting Habits of Female Anophelines in West Africa.** *Bull. Entom. Res.* 1946, Feb., v. 36, Pt. 4, 395–415, 3 figs. [13 refs.]

The experiments were carried out in a village near Freetown, Sierra Leone, and at Krabonekrom, near Sekondi, Gold Coast. The author throughout compares his findings in West Africa with those obtained by HADDOW [this *Bulletin*, 1942, v. 39, 595] in Kenya. All catches were made by collecting mosquitoes after spraying the room with a pyrethrum-in-kerosene mixture. In order to avoid any repellent effect, a series of identical huts were used and the human bait was shifted to a fresh house after each catch. Ribbands

considers that if this precaution is used the spray method is more efficient than the hand-catching employed by Haddow.

In West Africa, female anophelines were virtually absent from unoccupied huts. The author suggests that the higher proportion found in such huts in Kenya may be the result of outdoor conditions, which in East Africa may be less favourable to adult anophelines. The great majority of *A. gambiae* and *A. funestus* which have fed in native houses, remain there until after dawn; the period which elapses after dawn before they finally leave the hut depends on the extent to which the interior of the hut is exposed to daylight. *A. melas* seldom left huts in which they had fed, if there was little light or ventilation, until after dark the following day.

As suggested by the title of the paper, Ribbands devoted considerable attention to the influence of moonlight on the house-haunting habits of West African anophelines, a subject which, so far as the reviewer is aware, has previously received but little attention. The results obtained proved a high degree of correlation between the time of moonlight and the time of entry of *A. funestus*; the figures for *A. gambiae* were inadequate, but the author suspects that a similar relationship probably exists. The following is quoted from that part of his summary concerned with the affects of moonlight: "During moonless periods, the flighting of ♀ *A. funestus* was partially inhibited, and when the moon came out, the waiting mosquitos entered the huts in greatest numbers. The average proportion caught when the moon rose during catching periods ending 10 p.m., midnight and 7 a.m. was approximately 50 per cent., 100 per cent. and 400 per cent. greater, respectively, than the proportion caught during these periods on moonless nights. On moonless nights many mosquitos waited until twilight of the following evening before entering the huts, and in consequence the average proportion caught in the period ending 8 p.m. was six times greater on moonless nights than on the nights after full moon.

"The records for ♀ *A. melas* are less complete, and the correlation coefficient for the relation between time of entry and time of moonlight has the value of $0{\cdot}421 \pm 0{\cdot}184$, a result which is barely significant. In view of the highly significant correlations found in the case of *A. funestus* it is unlikely that this correlation is fortuitous."

The author considers that, in view of the high correlation which he has shown to exist between the time of moonlight and the time of flighting, it would be useless to compile records of the average time of entry into houses unless either the readings were sufficiently numerous to cancel out the effects of the lunar cycle, or else weighted averages of percentage catches were used. With the latter method he obtained the following results:—

"The average rate of entry of ♀ *A. funestus* throughout one complete lunar cycle at Krabonekrom, Gold Coast, was 27 per cent. before 8 p.m., 22 between 8 p.m. and 10 p.m., 21 between 10 p.m. and midnight and 30 after midnight. The similar rates for *A. gambiae* (based on very few records), were 10, 20, 30 and 40 per cent. respectively. Comparable rates for *A. melas* in Sierra Leone are not available, but at least 45 per cent. entered before 10 p.m. (=11 p.m. Gold Coast time)."

As regards the time of feeding, Ribbands's observations show that in West Africa, anophelines usually rest on the wall of the hut for some little time before commencing their meal. Thus, although 27 per cent. (figures based on *A. funestus*) of anophelines entered houses before 8 p.m., 58 per cent. of those caught at 8 p.m. were unfed; whereas of the anophelines caught in huts after dawn, 95 per cent. were fully fed. The author points out that this may explain how residual DDT on walls is able to protect the occupants of the room against biting, since the mosquitoes are incapacitated during this preliminary short resting period.

[This is a most useful and interesting paper, which should be consulted in the original by those concerned.] *R. M. Gordon.*

GIUA, A. Comportamento della citopoiesi midollare nei bambini malarici. [**Cell Production in Bone Marrow of Malarious Children.**] *Haematologica.* Pavia. 1945, v. 27, 399–435, 8 figs. [69 refs.] French summary.

ECKSTEIN, A. & NIXON, W. C. W. **Congenital Malaria.** *Brit. Med. J.* 1946, Mar. 23, 432–3.

With wide experience of malaria in Turkey the authors contend that congenital malaria is not uncommon in places where the disease is endemic. They cite five cases. [The ages of these infants ranged from 2 to 3 weeks, so the possibility of infection after birth cannot be altogether excluded, though this seems to have been unlikely in some cases.] All five mothers were suffering from malaria. Three were *P. vivax* infections, two *P. falciparum.* One of the infant patients was one of twins ; the other twin also harboured *P. vivax* but presented no clinical signs of infection other than some enlargement of the spleen. It is suggested that high infant mortality rates might be reduced if mothers received adequate suppressive and prophylactic treatment during pregnancy. *Norman White.*

MAKARI, J. G. **The Cephalin Flocculation Test in Malaria.** *Brit. Med. J.* 1946, Feb. 23, 272–3, 2 figs.

The cephalin-cholesterol flocculation test was first described by HANGER (*Trans. Ass. Amer. Phys.*, 1938, v. 53, 148) and has since proved its value as a test of hepatic function. The author applied it in 105 cases of malaria. A positive flocculation reaction was obtained in 96 cases (91·4 per cent.) ; in 94 of these the reaction was ++ or above. Both *P. falciparum* and *P. vivax* infections were included. The reaction tended to become negative with antimalaria treatment. It is suggested that the test might be used on cerebrospinal fluid in cerebral malaria, to determine the degree of activity of the infection, and that it might be used as a routine on prospective blood donors.

Ninety persons in whom there was no evidence of either malaria or liver disease were also examined ; in all the cephalin flocculation test was negative. *Norman White.*

JENNINGS, G. H. **Coma as Onset in a Case of Malaria in England.** [Memoranda.] *Brit. Med. J.* 1946, Apr. 27, 650.

The patient, a man aged 23, had lived in West Africa for 11 months, during which he had taken 10 grains of quinine daily as a prophylactic [presumably effective] against malaria, but had discontinued taking it on leaving for England. A few days after his arrival in England he had had two very short attacks of " fever ", and felt apathetic and rather sleepy during the following six weeks ; for a week before his admission to hospital he had been treated at his home for anaemia. He complained of pain in his right arm 24 hours before admission, and on the evening of the next day coma with high fever (105°F.) developed suddenly and he was admitted to hospital.

*Condition on admission.*—Temperature 104·2°F. ; respiration 36, deep and noisy ; pupils moderately dilated, not reacting to light ; no neck rigidity ; tendon jerks much exaggerated, bilateral ankle clonus present, plantar reflexes extensor, abdominal reflexes absent ; spleen 3 inches below the ribs ; blood showed numerous subtertian malarial parasites.

*Course and treatment.*—He was given quinine bihydrochloride, 20 grains intravenously and, later, tepid sponging; his temperature fell and he quickly recovered consciousness. Next day he was bright and alert but very pale; the spleen was undiminished in size; the blood showed Hb. 40 per cent., R.B.C. 1,720,000, C.I. 1.17, W.B.C. 3,260, (P. 52 per cent., L. 40 per cent., M. 8 per cent.). He was given quinine bihydrochloride 10 grains t.i.d. and mepacrine 0·1 gm. t.i.d. for two days, then quinine bihydrochloride 5 grains t.i.d. and ferri et ammon. cit. 40–90 grains daily. Six days after admission the spleen was no longer palpable and the abdominal reflexes were normal, but the tendon jerks in the legs were still slightly exaggerated. After taking a 5-day course of pamaquin 0·02 gm. t.i.d., he was discharged on the 17th day after admission; his blood then showed Hb. 70 per cent., R.B.C. 3,860,000, C.I.O. 92, W.B.C. 6,400 (P. 72 per cent., L. 20 per cent., M. 7 per cent., E. 1 per cent.). His temperature became normal after the second day. Two months later he showed no anaemia and had had no relapses. *J. F. Corson.*

PARRY, E. **Surgery in Malaria.** *Lancet.* 1946, Jan. 12, 49–51.

In many cases of *P. falciparum* infection there is a tendency to haemorrhage. Such haemorrhage can lead to mistakes in diagnosis. It was the outstanding characteristic of eight interesting surgical cases cited by the author, in all of which the prompt recognition of a coexisting *P. falciparum* infection and the prompt intravenous administration of quinine were quickly followed by cessation of bleeding. The cases include a compound fracture of both bones of the leg; a penetrating wound of the neck; a fracture of the pelvis with rupture of the urethra; profuse epistaxis; two cases of haemorrhage into adenomata of the thyroid; and a case of appendicitis in which numerous subserous petechial haemorrhages in visceral and parietal peritoneum were attributable to malaria infection. Malaria is liable to concentrate on the lungs after an inhalation anaesthesia just as it tends to cause cerebral malaria after intravenous anaesthesia.

The author states that to anyone who has been in the far-eastern theatre of war since its beginning, the beneficial changes wrought by mepacrine in the treatment of malaria are little short of miraculous. *Norman White.*

DOLE, V. P. & EMERSON, K., Jr., with the technical assistance of Esther BRAUN. **Electrophoretic Changes in the Plasma Protein Patterns of Patients with Relapsing Malaria.** *J. Clin. Investigation.* 1945, Sept., v. 24, No. 5, 644–7, 1 fig.

The total protein, albumin and globulin content of the plasma of eight patients suffering from *P. vivax* malaria was measured during the clinical attack after the patients had been allowed three paroxysms, and at varying times subsequently. The albumin and globulin fractions were estimated by electrophoresis and by salt fractionation.

The authors found that during the malarial attack the total protein remained within normal limits. The albumin/globulin ratio was depressed. The increase in globulin occurred mainly in the fibrinogen and $\gamma$ globulin fractions. The mobility of the protein was normal during the malarial attack. The plasma protein content returned to normal after specific treatment and during the inter-relapse period.

In a single case of *P. falciparum* malaria which was untreated for 3 weeks, the total protein dropped to 3·64 gm. per cent. [normal value 6·7], with an albumin globulin ratio of 1·3 (salt fractionation) or 0·72 (electrophoretic).

The author considers that the changes in plasma protein are not specific in malaria. Consequently, methods of diagnosis based on the protein pattern are not reliable in malaria [see PROSKE & WATSON, this *Bulletin*, 1939, v. 36, 813], particularly as the pattern returns to normal between relapses, although the infection with *P. vivax* must persist during this period.

[The authors do not attempt to relate the protein pattern to the effects of treatment, although their figures show that in one case treated with atabrine (mepacrine) the plasma protein reached a maximum concentration during treatment, whereas in another case treated with quinine, the protein was depressed during treatment and rose to a maximum after treatment was finished.] *B. G. Maegraith.*

LE CHUITON, F. La prophylaxie et le traitement du paludisme dans la marine. [**The Prophylaxis and Treatment of Malaria in the French Navy.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 1/2, 36–43.

SIMPSON, J. C. E. & SCHOFIELD, K. **Antimalarial Action of Cinnoline Derivatives.** [Correspondence.] *Nature.* 1946, Apr. 6, 439–40.

KELSEY, F. E., OLDHAM, F. K., CANTRELL, W. & GEILING, E. M. K. **Antimalarial Activity and Toxicity of a Metabolic Derivative of Quinine.** [Correspondence.] *Nature.* 1946, Apr. 6, 440.

YUDKIN, J. **Urinary Mepacrine in relation to Incidence and Diagnosis of Malaria.** *Lancet.* 1946, Mar. 16, 377–80, 1 chart.

This paper describes the results of estimation of urinary mepacrine in groups of healthy European Service personnel in W. Africa with different malarial incidence (all malignant tertian) and in unselected patients admitted to hospital there. All the subjects were supposed to be having 0·7 gm. of mepacrine weekly as a suppressive. For estimation the method of YUDKIN [this *Bulletin*, 1945, v. 42, 863] was employed. Since there is a relationship between the amount of mepacrine excreted in the urine and its level in the blood, the amount of drug excreted in unit time might therefore be related to the incidence of malaria. As completely reliable 24-hour specimens of urine could not be obtained, 3-hour specimens were used. It was found that the lowest excretion of drug occurred in the group of subjects with highest incidence of malaria. For practical reasons a method was developed in which random samples of urine were used for the estimation of mepacrine excretion. Output depends on concentration of drug, as well as on the volume of urine passed, and the latter has an influence on the specific gravity of the sample. To estimate the output of mepacrine, its concentration in a random sample of urine was determined and also the specific gravity of the specimen. The concentration value for a urine of sp. gr. 1·010 was then calculated, and the author terms this latter value—the "standard" urinary concentration of mepacrine. It was found that figures for the relative excretion of mepacrine in individuals, or in groups, were similar when estimated either as standard concentration or as total output over a period. The concentration of mepacrine was measured by the former method in 149 cases divided into four groups as follows—(1) proved malaria; (2) clinical malaria (no parasites seen in blood but signs and symptoms suggestive); (3) other medical conditions; (4) surgical conditions. In cases of proved malaria the excretion of mepacrine was found to be low. The author believes that a high excretion of mepacrine should exclude a diagnosis of malaria. From his own and other evidence he concludes that a

high proportion of cases diagnosed as clinical malaria are in fact not malaria. [This is in contrast to the experience of HYMAN (this *Bulletin*, 1945, v. 42, 962) in South Pacific Areas.] *J. D. Fulton.*

ELLERBROOK, L. D., LIPPINCOTT, S. W., CATENO, C. F., GORDON, H. H. & MARBLE, A. **Plasma Quinacrine Concentration in Treatment of** *Plasmodium vivax* **Malaria acquired in the South Pacific.** *Arch. Intern. Med.* 1945, Nov.–Dec., v. 76, No. 5, 352–7, 7 figs.

Mepacrine (quinacrine) was estimated by the method of BRODIE and UDENFRIEND [this *Bulletin*, 1943, v. 40, 821]. When known amounts were added to plasma, an average recovery of 96 per cent. (82–110 per cent.) was obtained. An average blank value of 3 micrograms per litre was observed in the plasma of untreated persons. Determinations were made on 6,733 specimens from 291 patients with relapsing malaria, treated in Texas. Doses were given with meals (at 7.30 a.m., 11.30 a.m. and 5 p.m.), and specimens for estimation were collected before breakfast. There were four groups of patients: Group I (54 patients) received 0·2 gm. orally at meals and at midnight for 5 doses, and then 0·1 gm. thrice daily until a total of 2·8 gm. had been received. The plasma concentration in this group is shown in Fig. 1 in which the heavy line represents the average for the group, and the two lighter lines indicate 1 standard deviation on each side of the mean (and include approximately 2/3 of all values). Patients in Group II received 2·8 gm. of mepacrine, given as in Group I. Then they were given a rest for 24 hours, and 0·01 gm. of pamaquin naphthoate thrice daily for 3 days, followed by 0·1 gm. of mepacrine on 6 days of the week until the sixtieth day from the start of treatment. Group III was similar, but the pamaquin was omitted. The plasma levels in these two groups were similar to those of Group I except that after the 14th day an approximately steady level of plasma mepacrine was maintained at 20–30 micrograms per litre. The average diurnal variation is shown in Fig. 2. In Group IV, 0·4 gm. of mepacrine was given at 9 a.m., followed by 0·2 gm. at 4.30 p.m. and at 1 a.m.; then 0·2 gm. was given at 9 a.m. and 9 p.m. for 6

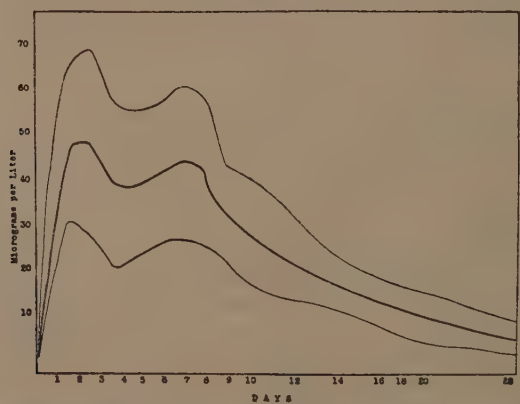



Fig. 1.—Fasting plasma quinacrine concentrations in 104 patients for eight days and in 54 patients thereafter (2·8 Gm. of quinacrine hydrochloride in one week). The heavy line indicates average values.

In Figs. 1 and 4 fine lines indicate 1 standard deviation (includes approximately two-thirds of all values).

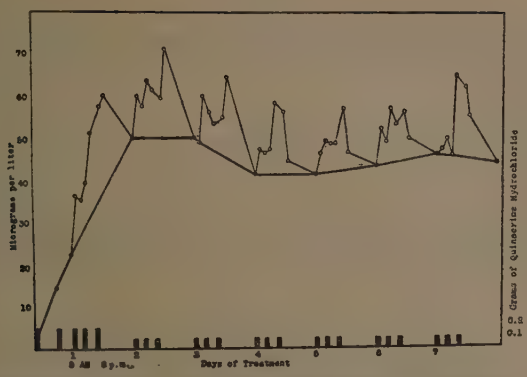



Fig. 2.—Diurnal variation of plasma quinacrine concentrations in 104 patients given 2·8 Gm. of quinacrine hydrochloride.

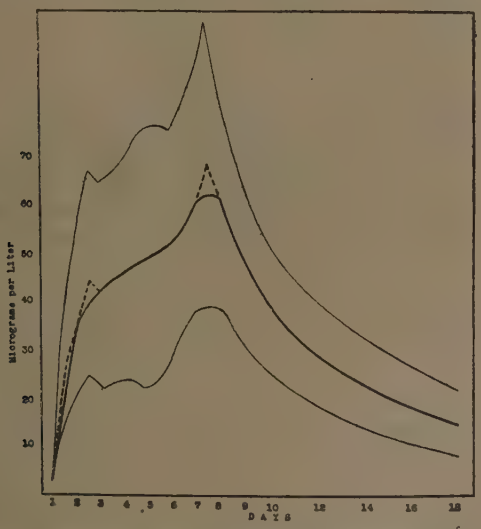



Fig. 4.—Plasma quinacrine concentrations of 35 patients who were given 3·2 Gm. of quinacrine hydrochloride in one week, The heavy line indicates average fasting values. The broken line indicates five hours after administration of 0·2 Gm.

[Reproduced from the *Archives of Internal Medicine.*]

days. The average plasma concentration of mepacrine is shown in Fig. 4. Under these treatments, pyrexia and other symptoms rapidly subsided and parasites disappeared from the blood. *F. Hawking.*

ABBEY, E. A. & LAWRENCE, E. A. **The Effect of Atabrine Suppressive Therapy on Eyesight in Pilots.** *J. Amer. Med. Ass.* 1946, Mar. 23, v. 130, No. 12, 786–7.

" 1. The continued use of atabrine in doses of one tablet (0·1 Gm.) a day appears to have no effect on visual acuity, except in a highly sensitive and rare individual.

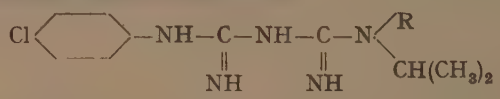
"2. Older persons on suppressive atabrine therapy do not differ from the younger group as far as visual acuity is concerned.

"3. There is no correlation between the depth of dermal discoloration and change in visual acuity.

"4. The depth of dermal staining appears to be as a result of individual sensitivity and not related to the length of time atabrine has been taken."

AUSTRALIAN ARMY MEDICAL RESEARCH UNIT, CAIRNS, QUEENSLAND (FAIRLEY, N. Hamilton, Director). **The Value of M4430 as a Suppressive Drug in Volunteers exposed to Experimental Mosquito-transmitted Malaria.** (*P. vivax*-**New Guinea Strains.**) (RFA (46) 5.) 1946, Mar. 11, 6 mimeographed pp., 1 chart.

In order to test the value of M4430 as a suppressive drug in benign tertian malaria, experiments have been carried out on similar lines to those with "Paludrine" (M4888) [this *Bulletin*, 1946, v. 43, 527]. The chemical constitutions of these substances are as follows :—



In "Paludrine" R=H ; and in M4430, R=$CH_3$.

Eight volunteers were exposed to the bites of *A. punctulatus* var. *punctulatus* recently infected with New Guinea strains of *P. vivax*. From the day previous to exposure, six received one 200 mgm. dose of M4430 daily by mouth. The seventh received 100 mgm. of mepacrine in the same way, following previous medication with 200 mgm. of this drug twice daily for four days. Administration of each drug was continued for a further 23 days. One volunteer, who received no therapy, acted as a control and became infected in the normal period. Routine clinical and laboratory examinations were made on each patient and nine days after the exposure to mosquito bites, subinoculations were made with 200 cc. of whole blood from the six receiving M4430. The results were negative in each case indicating that erythrocytic forms had not been liberated from [postulated] e.e. forms in the normal way. During treatment with either drug parasites were not found in the blood, and all the patients remained well. Malaria developed 16–59 days after treatment ended in the six cases receiving M4430 and after 27 days in the patient who received mepacrine. These results indicate that the e.e. forms were not eradicated, and that the new drug acts as a partial causal prophylactic against infection with New Guinea strains of *P. vivax*. The eight volunteers with overt malaria were now treated with 400 mgm. of M4430 daily for 14 days. Their blood became free from asexual parasites in 6–10 days after treatment started, and symptoms lasted, on an average, for 5 days. In view of the fact that the dose of the drug was small [ADAMS *et al.*, this *Bulletin*, 1946, v. 43, 400–401, gave up to 500 mgm. thrice daily], that treatment was started late, and that clinical and laboratory criteria were very exacting, the authors considered the schizonticidal action of M4430, which resembled that of "Paludrine," to be satisfactory, and probably equal to that of quinine or mepacrine. Three months after treatment ended, none of the patients had relapsed. Toxic symptoms due to the drug were not observed. *J. D. Fulton.*

JONES, H. A., LINDQUIST, A. W., DEONIER, C. C. & HUSMAN, C. N. **Dispersion of DDT Sprays from Fast Combat Aircraft.** *J. Econom. Entom.* 1945, Dec., v. 38, No. 6, 691–3.

COATNEY, G. R., COOPER, W. C. & TREMBLEY, Helen L. **Studies on *Plasmodium gallinaceum* Brumpt. III. The Incidence and Course of the Infection in Young Chicks following the Subcutaneous Inoculation of Pooled Sporozoites.** *Amer. J. Hyg.* 1945, Nov., v. 42, No. 3, 323–9, 1 fig.

In the first two papers of this series [this *Bulletin*, 1945, v. 42, 865] the course of *P. gallinaceum* infections in young chicks induced by the bite of a single infected mosquito (*Aëdes aegypti*), or the injection of a single infected salivary gland, were considered. In the present paper the infections in 2 to 5-day-old chicks resulting from the subcutaneous injection of serum-saline emulsions of entire infected mosquitoes are described. In practice an emulsion of a number of mosquitoes was made at one time, the exact number being determined by the number of chicks to be injected and the percentage of infected mosquitoes in the particular batch employed, as proved by previous dissection of samples. The number of mosquitoes emulsified was such as to give one infected mosquito for each chick. The paper gives the data obtained from 440 chicks infected in this manner. The incidence of infection was 99·8 per cent. with a mean prepatent period of 7·82 ± 0·043 days. The mean peak parasitaemia occurred 2·31 ± 0·053 days after patency and the mean peak parasite count was 3,439 ± 89 parasitized cells per 10,000 red blood corpuscles. Of the 439 infected birds 432 (98·4 per cent.) died, the mean survival time after the first patent day being 3·40 ± 0·064 days or 11·21 ± 0·082 days after the day of infection. Seven birds (1·6 per cent.) survived to develop chronic infections. Brain smears of 204 of the 432 chicks dying of the infection were examined. All showed exoerythrocytic forms. The results show that the method of infecting chicks employed in these experiments is less time-consuming than other methods. Furthermore it produces infections more certainly and these are more likely to result in early death. The method is the one of choice where screening tests on a large number of drugs have to be carried out. *C. M. Wenyon.*

TALIAFERRO, W. H., TALIAFERRO, Lucy G. & SIMMONS, E. L. **Increased Parasitemia in Chicken Malaria** (*Plasmodium gallinaceum* **and** *Plasmodium lophurae*) **following X-Irradiation.** *J. Infect. Dis.* 1945, Sept.–Oct., v. 77, No. 2, 158–76, 6 figs. [27 refs.]

Infections of *P. gallinaceum* in chickens are characterized by an increase of the parasites up to a peak and, if not fatal or checked by quinine, a decline in intensity and a passage into a condition of developed infection in which parasites are present in the blood almost continuously for several months. Infections of *P. lophurae*, on the other hand, show a rapid rise in the number of parasites in the blood followed, if survival occurs, by a rapid fall to a condition of latency in which parasites cannot be found in the blood. Associated with these differences are different responses to X-ray irradiation. In *P. gallinaceum* infections induced by blood or sporozoite inoculations, irradiation on the day of injection with 500 to 600 r results in an increase of the parasitaemia and a significant decrease in the survival time. If the exposure is made during the acute rise, or at the time of the crisis of infections the severity of which had been checked by quinine, there follow fatal infections which would not otherwise have occurred. Exposure during the period of developed infection was followed by relapses. In the case of *P. lophurae* infections irradiation on the day of injection is followed by fatal infections, but exposure at other times results in only slight relapses. It was found that the effectiveness of any given dose of X-rays varied with the age and susceptibility of the chickens, the species of parasite employed, the stage of the malarial infection and the intensity of the infection before and at the time of the irradiation. All these variations appear

to be related to natural and acquired immunity which would be modified by the destruction of lymphocytes, which irradiation brings about.

*C. M. Wenyon.*

RIGDON, R. H. & VARNADOE, Nona B. **Transfusions of Red Cells in Malaria. An Experimental Study in Ducks.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 409–15, 5 figs. [11 refs.]

In young ducks *Plasmodium lophurae* infections usually terminate fatally with low counts of both the red blood corpuscles and parasites. The parasites increase during the course of about a week to reach a peak in which the blood shows from 355 to 490 infected cells for 500 red cells. Shortly before the peak is reached the number of red cells begins to diminish rapidly, to fall in the course of 48 hours to 500,000 per cmm. From 2 to 24 hours after the commencement of the fall in the red cells, the diminution in the number of parasites begins. Not infrequently, following the commencement of the fall in the parasite count, there is a short rise in the count which does not usually reach the initial peak. In the case of the occasional duck that survives, the parasites disappear from the blood, while there is a rapid increase in the red cell count, which reaches normal in about a week. If infected ducks are transfused with normal duck blood in sufficient amounts to maintain the red cell count at its normal level, it is found that the parasite count also remains high. The transfusion thus not only postpones the advent of the anaemia but also delays the fall in the parasite count. This result is reached only if the quantity of normal blood is adequate, *e.g.*, 5 transfusions of 5 cc., and 4 of 10 cc. in 48 hours. If the quantity is less than this the course of the infection is unaffected. Though transfusion may not save the life of the ducks, its immediate effect is a marked improvement in health, which is most evident in the most anaemic. It is generally supposed that phagocytosis is mainly responsible for the fall in the parasite count which occurs after the peak has been reached. The authors consider that if this were true the parasite count should not be maintained by transfusion, which would not be expected to prevent phagocytosis from progressing normally. They suggest that factors other than phagocytosis may be significant in producing the decrease in the parasite count which follows the peak of the infection.

*C. M. Wenyon.*

TALIAFERRO, W. H. & BLOOM, W. **Inflammatory Reactions in the Skin of Normal and Immune Canaries and Monkeys after the Local Injection of Malarial Blood.** *J. Infect. Dis.* 1945, Sept.–Oct., v. 77, No. 2, 109–38, 7 pls. [25 refs.]

The object of the experiments described in this paper was the study of the local reactions when small quantities of malarial blood were inoculated subcutaneously (canaries) or intracutaneously (monkeys) into normal and immune canaries and monkeys. The malarial parasites involved were *P. cathemerium* for the canaries, *P. brasilianum* for cebus and spider monkeys, and *P. knowlesi* for rhesus monkeys. Control experiments were carried out by injecting normal blood or trypan blue. Conclusive evidence was obtained that the reaction was much more marked with *P. knowlesi* than with the other parasites. Thus red cells containing large stages of *P. knowlesi* were agglutinated and localized in the skin of immune rhesus monkeys, but were not agglutinated at all in normal rhesus monkeys. In addition, inflammation, including phagocytosis by heterophiles* and macrophages, was more marked in the skin of immune than of

* Heterophile leucocytes in man and in the above species of monkeys are the polymorphonuclear neutrophiles; the granules are more acidophile in the guineapig, rabbit and canary and were called pseudo-eosinophile. See MAXIMOW & BLOOM, "Textbook of Histology", 1942, 4th Ed., Saunders, pp. 47 & 48.—*Editor.*

normal rhesus monkeys. In contrast, inflammation was less marked in immune canaries, cebus monkeys and spider monkeys, while agglutination did not occur. It would seem that the marked reaction in immune rhesus monkeys is due to the great content of circulating antibody which allows effective amounts of this substance to leave the blood and enter the inflamed area. In both immune and non-immune monkeys and canaries, skin reactions to injections of malarial blood or trypan blue proceeded more rapidly than do the reactions in the skin of rats following the injection of trypan blue as described by the MÖLLENDORFFS and MAXIMOW. *C. M. Wenyon.*

KNISELY, M. H., ELIOT, T. S. & BLOCH, E. H. **Sludged Blood in Traumatic Shock. I. Microscopic Observations of the Precipitation and Agglutination of Blood flowing through Vessels in Crushed Tissues.** *Arch. Surgery.* 1945, Nov.–Dec., v. 51, No. 4, 220–36, 1 fig. [Refs. in footnotes.]

This paper contains a further report on the direct microscopic examination of blood and small vessels in living frogs and mammals, under normal conditions and following damage by crushing, and also in stage III of acute *P. knowlesi* malaria in monkeys [see also this *Bulletin*, 1943, v. 40, 584].

Under control conditions the authors observed that circulating red cells travel free inside the vessels and do not agglutinate, and that white cells do not stick to the vessel endothelium.

In stage III of *P. knowlesi* infection, a thick glassy precipitate forms between and around the red cells, the precipitate forming simultaneously in about 20 minutes throughout the whole body. The precipitate binds the cells together in "wads and masses (*not rouleaux*)," the circulating blood coming to resemble "sludge". This sludge resists its own flow through the small vessels, so that "stagnant anoxia" develops, the affected endothelium ultimately allowing fluid to leak into the tissues, with steady loss of intravascular fluid volume. Anoxia of the endothelium, alone, is sufficient to cause this. The red cells in *P. knowlesi* infection are not sticky to the endothelium, but are apparently sticky to the phagocytes of the liver, bone marrow and spleen, which readily ingest them, so contributing towards the malarial anaemia.

The authors consider the precipitate to be fibrin or something similar to it, and devised experiments to observe the effect of the introduction of freshly-formed fibrin into the circulation. For this purpose they observed the behaviour of blood cells and vessels in living animals after crushing trauma of various degrees, first in the omentum and then in muscle. They found that after crushing there were, in general, three regions of injury :—

(*a*) A zone in which small vessels are thrombosed ; no sludge is poured into the venous system.

(*b*) A "sludging zone", in which each venule pours out sludge into the general circulation, such out-pouring going on for long periods.

(*c*) A zone in which there is insufficient injury to cause any detectable change in the circulating blood.

The authors conclude that "when they are crushed striated and smooth muscles release substances capable of diffusing in through the vessel walls and reacting with constituents of the blood flowing through the patent vessels."

[This important paper should be read in the original by those who are interested in the vascular phenomena associated with shock-like conditions].

*B. G. Maegraith.*

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## BLACKWATER FEVER.

GEAR, J. **Autoantigens and Autoantibodies in the Pathogenesis of Disease with special reference to Blackwater Fever.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 301–14. [24 refs.]

The author states that in previous unpublished experiments he found that, whereas an emulsion of homologous liver produced no liver-antibodies when injected into rhesus monkeys (whether normal or protected by vaccine against yellow fever), an emulsion of liver from a rhesus monkey dead of yellow fever produced liver antibodies after injection into a rhesus monkey protected by vaccine against yellow fever. These results are similar to those obtained by SCHWENTKER and COMPLOIER (*J. Exper. Med.*, 1939, v. 70, 223) who reported the production of complement fixing antibodies reacting with both rabbit kidney and brain following the injection of emulsions of homologous kidney plus staphylococcal or streptococcal toxins into the rabbit.

On the strength of these observations the author suggests that the lysis of red cells in blackwater fever may result from the action of an autolysin produced in the following manner :—

i. Red cell+malaria parasite
or ,, ,, + ,, ,, +antimalarial drug } =auto-antigen.
or ,, ,, +antimalarial drug

ii. Auto-antigen+reticulo-endothelial system=auto-antibody (haemolysin).
iii. Red cell+haemolysin=sensitized red cell.
iv. Sensitized red cell+complement=lysis.

The theory is best expressed in the author's own words :—

" Red cells infected with malarial parasites, possibly only after treatment with an antimalarial drug or red cells altered by or combined with an antimalarial drug, become autoantigenic, and in response to this autoantigen an antibody or haemolysin is produced by the reticulo-endothelial system, particularly by the spleen. The titre of this haemolysin is boosted by each repeat attack of malaria. When the circulation of the blood through the spleen is free, this haemolysin is mopped up by the red cells and these sensitized red cells are removed by the reticulo-endothelial cells as they are sensitized and before a demonstrable intravascular haemolysis occurs. However, when the circulation through the spleen is impeded, and the spleen becomes congested, as it does in an attack of malaria, which also provides a secondary stimulus to boost the titre, this haemolysin accumulates. Factors which cause a sudden contraction of the spleen, such as the administration of quinine [*sic*], chill, and exertion, now would suddenly express into the general circulation sufficient haemolysin to sensitize a large number of red cells and their haemolysis intravascularly would result in haemoglobinaemia and haemoglobinuria, followed by the other signs and symptoms of blackwater fever."

The relevant literature on blackwater fever is reviewed. Points which the author considers to be in favour of his hypothesis are :—

(*a*) The occurrence of erythrophagocytosis, autoagglutination and spherocytosis in blackwater fever (all suggesting the presence of antibodies).

(*b*) The experiments of FOY *et al.* [this *Bulletin*, 1942, v. 39, 266 ; 1945, v. 42, 634] in which it was found that normal red cells injected into blackwater fever circulation and, conversely, red cells from an actively haemolysing blackwater fever patient injected into a normal circulation, were rapidly destroyed.

(*c*) The analogous effects produced by artificial lytic sera.

(*d*) The time lag between the first attack of malaria and the onset of blackwater fever, which suggests a process of sensitization.

[The arguments in this paper are facile but not altogether convincing in some respects. Nevertheless, it is a valuable paper, the importance of which is perhaps best expressed in the words of Schwentker and Comploier (1939, referred to by Dr. Gear) . . . "the entire theory discussed here is based on only a frail foundation. However, what evidence there is supports it as a possibility. Its value lies in offering a basis for further experimental work."]

*B. G. Maegraith.*

SINGH, I. & SINGH, I. **A Further Note on the Treatment of Black Water Fever with Antivenene.** *J. Indian Med. Ass.* 1946, Feb., v. 15, No. 5, 147–8.

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## TRYPANOSOMIASIS.

GALLAIS, P. Les formes neuro-psychiques de la trypanosomiase humaine africaine. (Essai d'une systématisation clinique et physiopathologique). [**The Neuropsychological Forms of African Human Trypanosomiasis.**] *Les Grandes Endémies Tropicales.* (Onzième Année.) 1939. Paris. pp. 113–51.

The symptoms and signs of African sleeping sickness are all well known but they have not yet been systematically grouped, and the author thinks that this explains why physicians outside tropical Africa often fail to diagnose the disease. In the nervous stage there is a general "family" resemblance among sleeping sickness patients. The disease is a diffuse meningo-encephalitis which, though it resembles syphilitic meningo-encephalitis to some extent, has special features of its own. Certain regions of the central nervous system are particularly affected and this gives it a clinical picture very different from that of general paralysis.

The fundamental neuro-psychical syndrome results from involvement of the region around the third ventricle—the hypothalamic region with the nuclei of the autonomous nervous system which are situated there. The symptoms may be classified as tropho-vegetative, psychic, motor, and sensory; these are described in considerable detail with notes of illustrative cases.

The author discusses the pathological lesions of the central nervous system; they are associated with the capillaries and the Virchow-Robin perivascular sheaths. He concludes that in trypanosomiasis there is a diffuse involvement of the walls of the cavities—the pia-arachnoid membrane with its prolongations, and the ventricular ependyma with the choroid plexuses, *i.e.* the parts where the cerebrospinal fluid is formed, circulates and is reabsorbed.

*J. F. Corson.*

BROWNING, C. H., CALVER, K. M., LECKIE, M. W. & WALLS, L. P. **Phenanthridine Compounds as Chemotherapeutic Agents in Experimental** *T. cruzi* **Infections.** [Correspondence.] *Nature.* 1946, Mar. 2, 263–4.

Prior to the present report there was only one compound known to exercise a favourable influence on *T. cruzi* infections, namely Bayer 7602 (Ac). [The reviewer has been informed by Dr. F. H. S. Curd, of Imperial Chemical Industries, Ltd., that previously published descriptions of the constitution of this compound, repeated in the article under review, are incomplete or incorrect. The true formula has now been published by H.M. Stationery Office in British Intelligence Objectives Sub-Committee (BIOS) Final Report No. 116, Item No. 24. Pharmaceuticals: Research and Manufacture at I.G. Farbenindustrie, page 53. It is diallylmalondi (4-amino-2-methyl-quinolyl-6-amide).]

The authors found that a number of phenanthridine compounds exhibit definite therapeutic activity against these infections in mice. In order to examine the matter properly, it was first necessary to determine accurately the course of untreated *T. cruzi* mouse infections, since these tend to be somewhat variable. The authors therefore passaged their strain, subcutaneously, as soon as parasites became numerous in the blood, since previous work with *T. congolense* had shown the advantages of using such an "acme" strain [BROWNING and CALVER, this *Bulletin*, 1945, v. 42, 259; CALVER, *ibid.*, 704]. In more than 140 such passages the trypanosomes became abundant in the blood in all but one case, and 82 per cent. of the mice died of the infection within 30 days, mostly between the thirteenth and nineteenth days. The remaining 18 per cent. showed a chronic course, surviving indefinitely, and parasites were scanty, or absent, for prolonged periods. Accordingly, in assessing the effect of treatment, it was necessary to allow for spontaneous suppression of the infection in a proportion equivalent to that shown by untreated controls.

Treatment consisted of one subcutaneous injection given as soon as scanty parasites appeared in the blood, and mice were reckoned as cured if trypanosomes disappeared from the blood permanently, either at once or after becoming numerous for not more than two or three days. The question of possible influence on the intracellular stage of the parasite was not examined.

Activity similar to that exhibited by Bayer 7602 (*Ac*), was shown by 3-carbethoxyamino-9-*p*-carbethoxyaminophenyl-10-methylphenanthridinium chloride (*S* 1544) and the corresponding, much more soluble, methanesulphonate (*S* 1577). The degree of activity, although the best yet encountered, is still not of a very high order.

It is interesting that the presence of a phenyl ring in the 9 position is not essential for activity, as was shown by a significant therapeutic response to 2 : 7-dicarbethoxyamino-9 : 10-dimethylphenanthridinium methosulphate (*S* 1582).

Immunity phenomena were believed to play a considerable part in the therapeutic effect, since cured animals and those showing suppression of infection failed to develop an obvious infection when reinoculated, even many months later. Nevertheless, unlike the case with *T. congolense* [BROWNING and CALVER; CALVER, *loc. cit.*] treatment is more successful at an early stage of infection than later, when parasites are numerous in the blood.

The above phenanthridinium compounds, which influence *T. cruzi*, do not affect *T. brucei* or *T. congolense* infections, except in high doses.

*E. M. Lourie.*

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## LEISHMANIASIS.

MORALES, A. L. Nuevas aportaciones a la quimioterapia del Kala-Azar infantil por el Solustibosán concentrado. [**Treatment of Infantile Kala Azar with Concentrated Solustibosan.**] *Rev. Sanidad e Hig. Pública.* 1945, Aug., v. 19, No. 8, 529–35.

The paper reports the successful treatment of ten cases of infantile kala azar in children up to five years of age, with concentrated solustibosan (sodium antimony gluconate). The drug was given intramuscularly in ten or eleven daily doses. In three cases the total quantity was 1 cc. per kilo. of body weight; in seven it was 1·5 cc. Better and more rapid results were obtained with the higher dosage, which was well tolerated by all the children. Treatment

commenced with an initial dose of 0·2 to 0·5 cc., according to the age and weight of the child; this was increased till a maximum daily dose was reached, which varied from 0·7 to 2 cc., Thus in a child 4 years old, weighing 14·5 kilo., the course consisted of 0·5, 1·0, 1·5, followed by nine doses of 2·0 cc.

*C. M. Wenyon.*

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## FEVERS OF THE TYPHUS GROUP.

OLITZKI, L., OLEINIK, E., CZACZKES, J. W. & KUTZENOK, A. **Thermostable Endotoxin of Rickettsiae.** [Correspondence.] *Nature.* 1946, Apr. 27, 552.

GROUPÉ, V. & DONOVICK, R. **Studies on Toxicity Complement-Fixing and Immunogenic Activity of Typhus-Infected Yolk Sacs.** *Proc. Soc. Exper. Biol. & Med.* 1945, Dec., v. 60, No. 3, 349–51. [10 refs.]

In the conditions described in the paper it was found that suspensions of yolk sacs, infected with the Breinl strain of epidemic-typhus rickettsiae, increased in toxicity in relation to the number of days of survival of the chick embryos from which the suspensions were prepared. Vaccines prepared from the suspensions showed a corresponding rise in antigenicity in relation to the survival period, and the complement-fixing activity of the antigens contained in the vaccines increased in the same way.

The toxicity experiments were carried out with untreated yolk-sac suspensions prepared from embryos still living on the 5th, 6th, 7th and 8th days, respectively, after inoculation, and it was found that certain dilutions of the 5th-day suspensions failed to kill any of the test mice, whereas corresponding dilutions of 8th-day suspensions killed all the test mice. The complement-fixing titres of these suspensions showed a corresponding degree of variation, being lowest in 5th-day suspensions and highest in 8th-day suspensions.

Vaccines were prepared from yolk sacs of embryos that died 5–7 days after inoculation, and from yolk sacs of embryos still surviving after 7 days; the results of tests of these vaccines are illustrated by the following examples:—

| | Vaccines prepared from embryos | | | |
|---|---|---|---|---|
| | D–5(1) | D–6 | D–7 | L–7(2) |
| Number of yolk sacs ... ... ... | 90 | 102 | 146 | 65 |
| Richness in rickettsiae ... ... ... | ± | + | ++ | ++++ |
| Complement-fixation at titre 1–64 ... ... | 0 | 2+ | 3+ | 4+ |
| Percentage of mice protected by 0·2 ml. of vaccine ... ... ... ... ... | 21·4 | 62·9 | No test | 85·7 |

(1) D–5 means dead after 5 days. (2) L–7 means still alive after 7 days.

The toxic and complement-fixing substances are not identical; the former are destroyed by formol and ether, which do not affect the latter, yet both are more active in yolk-sac suspensions of long-surviving than of short-surviving embryos.

*John W. D. M'egaw.*

DONOVICK, R., FARRELL, Mary & SMITH, Florence. **The Antibody Response of Guinea Pigs to Epidemic Typhus Vaccines of various Antigenicities.** *J. Bacteriology.* 1945, Sept., v. 50, No. 3, 241–7, 3 figs.

In this investigation, 48 lots, each consisting of 12–20 guineapigs, were vaccinated with two doses of one of 43 different batches of epidemic-typhus

vaccine, the sera of each lot of animals were collected and pooled 14 days after the administration of the second dose of vaccine. The antigenic titres of the vaccines ranged from 1–8 to 1–32. The antibody titres of the sera were tested by complement-fixation and mouse-neutralizing tests, and were found to correspond broadly with each other and also with the antigenic titres of the vaccines employed in immunizing the animals.

The authors conclude that a direct determination of the antigenic titre of the vaccine by the complement-fixation test appears to give an accurate measure of its protective value for guineapigs.

The general trend of the findings can be seen from the following analysis of the tables contained in the paper :—

*Antibody Titres of Sera of Pools of 12–20 Vaccinated Guineapigs.*

| Antigenic Titre of Vaccine | No. of Pools | Complement-Fixation Titres | | | | Mouse-Neutralizing Titres | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Range | 1–8 or less | 1–16 | 1–32 or more | Range | 1–8 or less | 1–16 | 1–32 or more |
| 1–8 | 13 | 1–4 to 1–32 | 5 | 6 | 2 | 1–8 to 1–32 | 4 | 6 | 3 |
| 1–16 | 19 | 1–4 to 1–128 | 6 | 8 | 5 | 1–8 to 1–128 | 6 | 5 | 8 |
| 1–32 | 16 | 1–8 to 1–256 | 1 | 4 | 11 | 1–8 to 1–64 | 2 | 4 | 10 |

Surprisingly great variations were observed in the antibody titres of different lots of animals immunized by the same vaccines ; in some cases the complement fixation titres ranged from 1–8 to 1–32, and in one case the mouse-neutralizing titre of pooled serum from one lot of 20 guineapigs was 1–128, whereas the titre of another lot of 20 that had received the same vaccine was 1–8. Even allowing for great variations in the susceptibility of individual animals it would not be expected that two lots of pooled serum, each obtained from 20 guineapigs selected at random and treated in the same way, should show such differences in their responses. The author feels compelled to suggest that it would be necessary to include 100 or more animals in each lot in order to obtain approximately similar responses with the pooled sera. *John W. D. Megaw.*

DE ALESSI, E. Epidemia di tifo esantematico in Grecia. [**An Epidemic of Typhus in Greece.**] *Giorn. di Batteriol. e Immunol.* 1943, Aug., v. 31, No. 2, 89–98. English summary (4 lines).

YEOMANS, A., SNYDER, J. C., MURRAY, E. S., ECKE, R. S. & ZARAFONETIS, C. J. D. **Azotemia in Typhus Fever.** *Ann. Intern. Med.* 1945, Nov., v. 23, No. 5, 711–53, 10 charts. [38 refs.]

The authors comment on the scantiness of the information available on the subject of azotaemia in the literature of typhus fever, and on the greatly conflicting views expressed by the few German and French workers who have studied the condition.

In the present investigation, 64 Egyptian patients were studied in the U.S.A. Typhus-Commission Ward of the Cairo Fever Hospital in 1943–44. It was soon found that the severest cases were in a condition of azotaemia, which was regarded as existing when the non-protein nitrogen of the blood was

45 mgm., or over, per 100 cc. Some of the patients affected were in a uraemic condition, some had pronounced hypotension, and some were severely dehydrated.

The incidence and degree of azotaemia among the patients is shown in the table, which has been compiled from data contained in the paper :—

| Severity of attack | No. of patients | No. having azotaemia | Maximum Non-Protein Nitrogen in Blood of Azotaemic Patients (mgm. per 100 cc.) | |
|---|---|---|---|---|
| | | | Average | Range |
| Very mild ... ... | 2 | 0 | — | — |
| Moderate ... ... | 14 | 4 | 58 | 47–74 |
| Severe ... ... ... | 26 | 9 | 69 | 58–117 |
| Very Severe ... ... | 7 | 5 | 92 | 72–162 |
| Fatal ... ... ... | 15 | 15 | 120 | 75–200 |

The average age of the 64 patients was 28 years ; of the 15 who died it was 33 years. There were no deaths among the patients who remained free from the condition. The average daily blood pressure was not lowered in the affected patients, but in many cases there was a sudden fall in the systolic pressure at the time of onset of the condition ; there was often also a diminution in the urinary output at this time ; azotaemia was rarely seen so long as the output remained above 2,000 cc. The time of onset was usually during the second week, but in a few cases it was before the 8th day. The specific gravity of the urine tended to be low, considering the reduction in the output. Dehydration, often associated with insufficient fluid intake, was regarded as an important contributory factor.

Albuminuria was present in all the cases ; red and white cells were often found in the urinary sediment ; cell casts were rarely seen, but granular casts were often present. After recovery it was exceptional to find evidence of renal damage ; this occurred in two cases, but the kidneys might have been affected before the attack.

Detailed reports, illustrated by charts, are given of ten cases, of which six were fatal. The investigation was exceptionally thorough, and the charts form a graphic record of the chief features of each case.

The cause of the condition is discussed at some length. In view of the above reference to deficient fluid intake and of the statement that inadequate intake of total calories is an important contributory factor, it is surprising to learn that the diet of most of the patients consisted of water, sweetened fruit juices, and 600 to 1,000 cc. of milk daily. [This diet, which is inadequate in proteins as well as in calories (as the authors themselves state), would not be expected to support the nutrition of the renal cells, the cardiac muscle, and the other tissues, already damaged by the infection. From the charts it appears that the daily fluid intake sometimes fell as low as two pints or even less. These circumstances, combined with the high virulence of the infection and the relatively low standard of nutrition of the patients before the illness, may account for the exceptional degree of frequency of the condition in the present series of cases. Other observers have recorded very different findings ; for example, SCHÄFER (this *Bulletin*, 1946, v. 43, 210) found no reading higher than 63 mgm. per 100 cc. during the second week among seven severe cases, and in the two of these that were fatal the readings were 21 and 35 mgm., respectively.]

*John W. D. Megaw.*

CRAUFURD-BENSON, H. J. & MACLEOD, J. **A.L.63, the Original British Army Louse Powder.** *J. Hygiene.* 1946, Jan., v. 44, No. 4, 294–306, 3 figs. [11 refs.]

This paper describes the work which led to the development of A.L.63, which was the official British Army louse powder from 1940 until the introduction of DDT in 1944. It was the only louse powder used by the British troops, and the civilians employed by the British army, during the Naples typhus epidemic of 1943–44. Except for two cases, where negligence was shown, there were no cases of typhus among the troops or among the 25,000 civilian employees treated at fortnightly intervals.

The problem was to develop a preparation for use by the individual which would (*a*) kill lice already present, (*b*) prevent infestation or re-infestation. The value of a preparation was established by laboratory scale tests, in which the lice were dusted and exposed to treated flannelette in bolting silk bottomed boxes worn on the leg during the daytime, and by practical tests with naturally lousy people in a specially established clinic in the East End of London. In the latter experiments the underclothes or specially provided shirts worn next to the skin were dusted.

All the dusts were made up with a kaolin base. The substances tested included among others pyrethrum, derris, naphthalene, high boiling tar acids and creosote, used alone and in various combinations. It was soon found that different results were obtained in the laboratory and field tests, and that, in general, higher concentrations of insecticide were necessary in the practical work.

Naphthalene killed the body lice most quickly but failed to give lasting protection. Derris and pyrethrum were toxic to lice, but either alone or mixed they were inferior to other insecticidal combinations. It was found that mixtures of high boiling tar acids and derris showed an activation effect, and such a mixture was more effective than either ingredient alone. This activated derris mixture was slow in action, but gave better lasting protection than other mixtures. By combining the rapid action of naphthalene with the lasting effect of derris activated with high boiling tar acids, formula A.L.63 was obtained, *i.e.* high boiling tar acids, 2 per cent. ; derris root, 14·3 per cent., giving 1 per cent. rotenone ; naphthalene 50·0 per cent. ; china clay 33·7 per cent. A.L.63 gave a 95 per cent. kill of lice present on treated garments at the time of application and protection from reinfestation for five days. When the subject was exposed in an infested environment it was found that retreatment at eight-day intervals gave effective protection. Applied as a prophylactic to clean garments, A.L.63 remained effective for seven to eight days and gave partial protection up to 16 days. *W. A. L. David.*

CRAUFURD-BENSON, H. J. **Naples Typhus Epidemic, 1942–3 [as seen by an Entomologist].** *Brit. Med. J.* 1946, Apr. 13, 579–80, 1 graph.

The epidemic of typhus in Naples during the winter of 1942–43 reached its maximum (300 cases a week) early in January, and then the number of cases fell rapidly. Previous experience would have led to the expectation that the number of cases would have gone on increasing to much higher levels during the early months of 1943, and there is little doubt that a dramatic result was obtained by the control measures described in this paper. These consisted of the mechanical application of louse powders to fully clothed individuals, a method which, though not immediately rendering them louse-free, enabled enormous numbers to be dealt with (2,759,000 individual applications up to April 1943). It also made those treated relatively " louse-proof ". Although

DDT is usually credited with the responsibility for the success achieved, it is here shown that the initial fall in incidence was mainly caused by the use of MYL, the American powder containing pyrethrum, and that the 20,000 civilian employees of the army were well protected by fortnightly dusting with the original powder, AL63, which contains derris and naphthalene. The later control was by means of DDT. *Kenneth Mellanby.*

WHEELER, C. M. **Control of Typhus in Italy 1943–1944 by Use of DDT.** *Amer. J. Pub. Health.* 1946, Feb., v. 36, No. 2, 119–29.

The author, a member of the U.S.A. Typhus Commission, describes the organization by which louse-borne typhus was promptly brought under control in Naples and Southern Italy in 1943–44. The remarkable success which was achieved in Naples ceases to be a matter of surprise to anyone who reads this report.

Preventive measures were started under the direction of the medical staffs of the Allied Forces, and later were controlled by the U.S.A. Typhus Commission.

As is shown by the title of the paper, chief reliance was placed on the use of DDT. This was used in the form of a 10 per cent. dusting powder, of which 1–1½ oz. was applied by hand-duster or by power-dusters to each person. The powder was blown between the skin and the inner layer of clothing and between the outer layers of clothing ; bedding and spare clothing in houses were also dusted when necessary.

The large team of workers employed was divided into a number of sections, (1) Case-Finding Section, (2) Contact Delousing Section, (3) Case Contact Service, (4) Special Services, (5) Ricovero (Air-Raid Shelter) Service, (6) Mass-Delousing Section, (7) Immunization Section, (8) Flying-Squadron Section ; later, (9) a Refugee Section was established to deal with groups of refugees from Yugoslavia and other countries. The Flying-Squadron Section attended to outbreaks reported from places outside Naples in southern Italy.

No adequate summary can be given of the work of the organization, especially as this was modified from time to time according to the needs of the situation. In a table it is shown that in Naples more than two and a half million dusting operations were performed, and in other places there were more than 600,000. The number of cases of typhus reported in Naples was 1,404 ; elsewhere in southern Italy there were 510 cases.

Within a month of the institution of control measures in Naples, on December 15th, 1943, a sharp decline in the number of cases set in, and by February 20th, 1944, the epidemic " appeared to have been definitely broken."

The Mass-Delousing Section was organized for the primary purpose of delousing the entire civilian population of Naples. It was planned on the basis of 50 stations equipped to dust as many as 100,000 persons daily. By February 8th, 40 such stations were working, with a combined staff of 439 persons.

The whole operation was a triumphant success, not only for DDT but also for the persons who planned and conducted the campaign.

*John W. D. Megaw.*

BEALL, J. C. **Permanent Program for Typhus Fever Control in Memphis, Tennessee.** *Amer. J. Pub. Health.* 1946, Feb., v. 36, No. 2, 161–8.

Readers outside the U.S.A. will probably be surprised to find that the " Programme for Typhus-Fever Control " described in this paper is purely one of rat control. The disease referred to is, of course, the one commonly called murine, or endemic, typhus, not louse-borne typhus.

In Memphis City a permanent organization has been set up with a view to preventing the disease from establishing itself, and apparently no cases had been reported till some months after the commencement of the planning of the campaign, when an outbreak of six cases occurred in a "feed mill" during August and September 1943.

In the month of November of the same year, the City Commissioners adopted an ordinance by which owners of all business premises were made responsible for keeping their buildings free from rats. The official organization included the purchase of initial equipment costing $8,000, but it was planned on a self-supporting basis and all owners were compelled to pay for the cost of the necessary operations, whether these were carried out by themselves or by the special section of the health staff. The personnel of the organization consisted of a public-health engineer, three field foremen, a sanitarian, and 22 negro labourers, of whom 12 were assigned to rat proofing, 8 to rat trapping and poisoning, and 2 to special work. The equipment included one motor car, three 1½-ton trucks, and one ½-ton truck.

Up to the time of writing, 299 business establishments had been dealt with at an average cost of $47·76 each. Apart from the compulsory powers provided by the ordinance, efforts were made to secure the willing co-operation of owners by a publicity campaign.

The residential area of the City has not yet come within the scope of the campaign, but plans are being made for the inclusion of these at a later date and for the compulsory inclusion of rat proofing of all new buildings.

The description of the organization will be found interesting by all concerned with rat control, though so high a standard of achievement would be unattainable in most of the places where the rat is a menace to public health.

*John W. D. Megaw.*

JOHNSON, D. H. & WHARTON, G. W. **Tsutsugamushi, Disease : Epidemiology and Methods of Survey and Control.** *U.S. Nav. Med. Bull.* 1946, Mar., v. 46, No. 3, 459–72, 1 fig.

This paper contains a useful summary of what is known of the epidemiology and prevention of tsutsugamushi disease. The word "chiggers" is defined as "the larvae of mites of the family trombiculidae," of which about 150 species are known, including at least 100 in the regions in which the disease occurs. A description is given of the characteristics by which these larvae can be distinguished from other minute arthropods.

Rickettsiae are believed to be introduced into the body of the host with the saliva, which is injected by the larvae, and which dissolves the tissues, so preparing them for ingestion. The larva, after its one and only meal, drops off and buries itself in the upper layers of the soil ; in the nymphal and adult stages the mite is non-parasitic, feeding on organic matter in the soil. When the larvae are hatched out they swarm actively on any object that disturbs their habitat.

Infection is believed to be transmitted through successive generations of mites, which may therefore be the real reservoirs of infection. But even if the animal hosts should be found to play no direct part in the transmission cycle, they would still be essential for the maintenance of the mite population. Many vertebrates serve as hosts ; wild rats are the most important, but ground-living birds are often bitten, and these when they migrate are likely to convey infected mites to distant places.

Many rats make their nests in places suitable as habitats for the mites. The infected areas, which may be strictly localized, are usually moist, but well-drained, and are covered with herbaceous and scrubby vegetation. Such areas are specially likely to be selected as sites for camps. Coconut and other food

trees or plants attract rats. Water-logged or dry soil, and dense jungle, are seldom infested by mites.

Directions are given for the trapping of rats and for the examination of these and the other vertebrate hosts for the detection of mites. Methods of protecting investigators from infection include the immediate immersion of trapped rats in 80 per cent. alcohol, ideally, or alternatively the temporary use of tight-lidded canisters; the wearing of impregnated clothing, frequent application to the hands and wrists of dimethyl phthalate, and the placing of the dead bodies of animals under examination on large trays smeared with dimethyl phthalate.

White porcelain cups were found suitable for collecting larvae; the cups were placed on the ground in contact with the surface litter for one to five minutes and then examined.

If larvae are found on small mammals the presence of infection should be suspected; abundant larvae on birds and reptiles are likely to be "pest jiggers" [larvae which cause scrub itch]. Identification of species is a matter for experts.

Soil can be disinfested by DDT, five to ten pounds of a 10 per cent. powder is enough for each acre. Dimethyl phthalate is used for personal protection, and also for spraying the floors of tents and huts when the slower action of DDT might not be adequate. Instructions are given for the impregnation of clothing and blankets with dimethyl phthalate, which remains effective for two weeks in the absence of repeated wetting by rain. Untreated shorts should be worn under the impregnated outer garments to avoid irritation of the genitalia. For the protection of one person, two ounces of dimethyl phthalate can be applied by the smear method, in which a few drops at a time are spread on the palms of the hands and rubbed on the socks and clothing by repeated applications till the whole surface has been uniformly treated.

The exposed skin is also smeared lightly, avoiding the lips and eyes.

Dibutyl phthalate, used by the smear method, is preferred by the Australian Army; its effect is slower but is said to be more persistent.

Rat control by trapping and poisoning is recommended [though in view of the authors' own account of the life-history of the mites the destruction of rats would not be expected to have an early effect in reducing the number of infected larvae, it might even in certain conditions increase the risk to human beings by depriving the larvae of their usual hosts.]

The vegetation of risky camp sites should be cut and removed; the stubble should be sprayed with Diesel oil or kerosene, and burned, or it may be dealt with by a flame-thrower. *John W. D. Megaw.*

CLANCY, C. F. & WOLFE, D. M. **A Rapid Staining Method for *Rickettsia orientalis*.** *Science.* 1945, Nov. 9, 483.

The following method of staining *Rickettsia orientalis* in smears from infected yolk sac membrane or other tissues gives good results and is quicker than that of SYVERTON and THOMAS [this *Bulletin*, 1945, v. 42, 879]. The smears are dried in air and fixed by heat; xylol is poured on, drained off, and the slide is again dried in air. It is then immersed for 5 minutes in a mixture of methylene blue and basic fuchsin—each 1 : 5,000 in distilled water—washed in tap water and dried. The dilute stain is best freshly prepared as required, *e.g.*, daily, from stock 1 per cent. solution of the two dyes. *J. F. Corson.*

O'CONNOR, J. L. **Hirst's Haemagglutination Phenomenon exhibited by** *Rickettsia orientalis* **(Syn. Tsutsugamushi).** *Med. J. Australia.* 1945, Dec. 22, v. 2, No. 25, 459–60.

Cultures of *Rickettsia orientalis* grown on the chorio-allantoic membrane of duck embryos caused agglutination of suspensions of red blood cells prepared from fowls, but positive results were obtained in only two of eight suspensions made from different fowls.

HIRST (*Science*, 1941, July 4, 22) [see also *Bulletin of Hygiene*, 1942, v. 17, 666] described the agglutination of red cells of fowls by influenza virus, and CLARK and NAGLER [*Bulletin of Hygiene*, 1944, v. 19, 164] found that the same phenomenon occurred with vaccinia virus, but only in about half of the red-cell suspensions that were tested.

In further experiments the author found that the serum of a patient convalescent from scrub typhus contained antibodies which inhibited the agglutination, and that embryonic ducks' erythrocytes adsorbed most of the infecting agent from infected allantoic fluid. No agglutination occurred in any of six samples of red-cell suspensions made from one-day-old chicks. One sample each of human, sheep, and guineapig cell suspensions also gave negative results. A description is given of the technical methods employed.

*John W. D. Megaw.*

DE BURGH, P. **The Use of a Polysaccharide of** *Bacillus proteus* **OXK in the Diagnosis of Scrub Typhus.** *Med. J. Australia.* 1946, Jan. 19, v. 1, No. 3, 81–3.

This study was undertaken to find whether *Proteus OXK* contained a polysaccharide-like substance corresponding to the one extracted by CASTAÑEDA and ZIA (1933) from *Pr. OX19*, and found by them to be a minor antigen common to *Pr. OX19* and *Rickettsia prowazeki*. The author extracted a polysaccharide from cultures of *Pr. OXK* by trichloracetic acid, after the method of BOIVIN (1933); and with a solution of this he sensitized collodion particles, prepared according to the technique of LOEB (1922). Details of the methods are given. Sera of two patients convalescent from scrub-typhus agglutinated the sensitized particles at the same titres (1–320 and 1–640) as were observed when *Pr. OXK* suspensions were used. The reaction is rapid, taking only 15 minutes. It appears to be more specific than the standard test, because among eight samples of normal sera there were seven which gave positive reactions at a titre of 1–40 with *Pr. OXK* suspensions, containing both the major and minor antigens; whereas there were no positives with the sensitized particles, containing only the minor antigen.

The suspensions of sensitized particles had "a life" of about one week in the ice-box. It is suggested that in certain conditions the advantages of the reaction may outweigh the drawback involved in the laborious method of preparation, and that other antigens, such as *Pr. OX19* may be used in the same way.

The polysaccharide was also used with success in a precipitin test, but this was less satisfactory than the agglutination test. *John W. D. Megaw.*

TRAVASSOS, J. & VALLEJO-FREIRE A. Criação artificial de *Amblyomma cajennense* para o preparo da vacina contra a febre maculosa [**Artificial Breeding of** *Amblyomma cajennense* **for the Preparation of Vaccine against São Paulo Spotted Fever.**] *Mem. Inst. Butantan.* 1944–1945, v. 18, 145–235, 32 figs. (3 coloured pls.) [36 refs.]

This interesting paper is really a monograph dealing with the preparation from ticks of a vaccine against the highly virulent São Paulo type of tick-borne typhus; it consists of 90 large pages of text illustrated by 32 figures and three good coloured plates.

The disease is an important public health problem in the rural areas of the State of São Paulo, where, since the discovery of the disease in 1929, hundreds of deaths have occurred in widely distributed areas, and in some places the disease interferes with the extension of agriculture.

Tick control was regarded as impracticable, so that an organization was established at the Butantan Institute in São Paulo for the production of a vaccine by the method worked out by SPENCER and PARKER for the closely related disease, Rocky Mountain spotted fever [see this *Bulletin*, 1926, v. 23, 361].

The pioneer worker on the vaccine in Brazil, MONTEIRO, and his assistant, Edison DIAS, died of accidental infections acquired in the laboratory.

The chief vector, *Amblyomma cajennense*, is the most abundant tick in the State and is also the easiest to rear in the laboratory; its life-history and identification are clearly described. Details are given of: (1) the method of breeding the tick on a large scale; (2) feeding the larvae on infected rabbits; (3) maintaining the infected ticks till they reach maturity; (4) the preparation and testing of the vaccine; and (5) the protection of workers from accidental infection. All these procedures are fully described, with the help of numerous photographic and other illustrations, which in themselves will be found very useful by those who undertake experimental work on ticks.

Little information is given about the output and distribution of the vaccine; and the authors admit that evidence of its efficiency in the field is very difficult to obtain. It is regarded as likely that vaccination, and six-monthly revaccination, give the same degree of protection as has been obtained by Spencer and Parker in Rocky Mountain spotted fever. The complete absence of laboratory accidents since the unfortunate fatalities mentioned above, is regarded as significant in view of the great risk of laboratory infection despite the elaborate precautions that have been taken. *John W. D. Megaw.*

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## YELLOW FEVER.

ANTUNES, W. & CASTRO, A. Zona endêmica da febre amarela no Brasil. [**Endemic Yellow Fever Area in Brazil.**] *Bol. Oficina Sanitaria Panamericana.* 1945, Nov., v. 24, No. 11, 972–9, 3 maps & 2 graphs. English summary.

The endemic yellow fever area of Brazil, based on experience of the last five years, includes: (*a*) all territory to the north of a line from the city of Brasília, Acre Territory, to Gurupí, in Pará, and thence along the Gurupí river to the Atlantic coast; (*b*) the districts of Ilhéus and Itabuna, at the east coast between the Contas and Pardo rivers. From the former area certain localities are excluded, *viz.*, Taraucá, Feijó, Sena Madureira, Xapurí, Brasília e Rio Branco, in Acre Territory; Porto Velho, in Guaporé Territory; Benjamin Constant, Tabatinga, São Paulo de Olivença, Fonte Boa, Tefé, Coarí, Codajaz, Manáus, Borba, Itacaotiara, Manicoré, Parintins, and Humaitá, in the State of Amazonas; Obidos, Santarém, Monte Alegre, Gurupá, Curralinho and Belém, in the State of Para.

The demarcation plan of UNRRA [this *Bulletin*, 1946, v. 43, 124] does not distinguish between endemic and epidemic areas; it includes a far larger area and would require periodical revision of the endemic areas to exclude quiescent epidemic areas. *J. F. Corson.*

GAST G., A. & BATES, M. La distribución estacional de fiebre amarilla humana y del mosquito *Haemagogus* en la intendencia del Meta (Colombia). [**The Seasonal Distribution of Yellow Fever and of *Haemagogus* in Part of Colombia.**] *Rev. Facul. de Med.* Bogota. 1945, Oct., v. 14, No. 4, 243–53, 1 graph. English summary.

" Field studies, confirmed by laboratory experimentation, indicate that the mosquito *Haemagogus capricornii* is the chief vector of yellow fever in eastern Colombia. The object of the present article is to compare the seasonal variation in abundance of this mosquito with the seasonal distribution of human yellow fever in the region of Villavicencio. The data for human yellow fever are based on the results of the examination of liver specimens obtained by the " Viscerotomy Service " over a period of 11 years. The data for mosquitoes are based on three years of standardized captures in a series of forest stations near Villavicencio.

" The climate of Villavicencio is relatively uniform through the year except for a dry season extending from December through March when rains are comparatively infrequent. Human yellow fever fatalities reach a minimum at the end of the dry season (March), and do not show a significant increase until the second month of rains (June) reaching a peak in November and December. Haemagogus mosquitoes become relatively scarce during the dry season, but the population increases rapidly after the onset of the rains, reaching a peak in June, showing a slow but steady decline for the rest of the year except for a slight increase in November. It seems likely that the scarcity of yellow fever in the dry season is dependent on the low population level of haemagogus mosquitoes, and the post-dry season increase in yellow fever lags about a month behind the increase in mosquitoes. Human yellow fever remains at a high level through the rest of the rainy season, even though the mosquito population is declining : and the peak of human yellow fever in November and December corresponds to only a slight rise in the mosquito population. It seems likely that the high incidence of yellow fever at this time is related to the habits of the local human population : it is customary to fell large areas of forest at this time, with the object of burning the land in January and February, leaving it ready for planting with the onset of the rains. The human population is thus in closer contact with the forest in November and December than at any other time of year."

LAEMMERT, H. W., Jr. **Studies on Susceptibility of Marsupialia to Different Strains of Yellow Fever Virus.** *Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 33–46. [10 refs.]

The susceptibility of marsupials to infection with yellow fever virus was investigated by BUGHER *et al.* [this *Bulletin*, 1941, v. 38, 434] and BATES [*ibid.*, 1944, v. 41, 749] ; in the present paper additional experiments with various strains of yellow fever virus and several species of marsupials are recorded. Altogether, 335 marsupials belonging to seven species were tested ; they were caught in various parts of Brazil, all except two of which were areas in which yellow fever was either epidemic at the time or had been reported previously.

The animals were of various ages, from newborn to adult, but most were young ; all were maintained satisfactorily under laboratory conditions. They were mostly inoculated subcutaneously, but other routes were used in some cases for comparison. The seven strains of yellow fever virus were : J.Z. (isolated in S. America in 1937) ; O.C. (S. America, 1940) ; M.D., J.A. & Martinez (S. American jungle strains) ; Asibi (Africa) ; and the French neurotropic strain (Africa). The J.Z. and O.C. strains, which had been isolated and maintained in *rhesus* monkeys, were mostly used.

The viruses were titrated by intracerebral inoculation of mice, and in the tests on marsupials small doses were inoculated as a rule. To test for circulating virus, blood was taken from the heart on successive days and the serum inoculated intracerebrally into mice ; in the cases of *Didelphis* and *Metachirops* the serum was diluted as it is toxic for mice. After 30 days the surviving marsupials were bled to test for specific antibodies ; no immune antibodies had been found before the inoculation of yellow fever virus.

The results of the tests are shown in seven tables from which, and from the text, the following details have been abstracted :—

| Species | Common name | No. | Circulating virus present in | Immune bodies developed in* |
|---|---|---|---|---|
| *Didelphis marsupialis* | Common opossum | 162 | 7 | 13/108 |
| *D. paraguayensis* ... | White-eared common opossum ... ... | 8 | 1 | 2/8 |
| *Metachirops opossum* | Grey-masked opossum | 68 | 15 | 11/41 |
| *M. nudicaudatus* ... | Brown-masked opossum | 44 | 26 | 25/36 |
| *Caluromys philander* | Woolly oposum ... | 12 | 11 | 8/9 |
| *Marmosa cinerea* ... | Murine opossum ... | 11 | 5 | 2/3 |
| *M. incana* ... | Murine opossum ... | 30 | 23 | 9/15 |

*The proportion of survivors which developed specific antibodies.

The author concluded that *D. marsupialis*, *D. paraguayensis* and *M. opossum* were resistant to the strains used, since only a few showed circulating virus and, in general, the immunity response was poor. South American opossums are aplacental animals and the author thinks it unlikely that the newborn animals (in the pouch) acquired passive immunity from the milk of the mothers. The results, in general, were similar to those of Bugher *et al.*, and Bates, but the former authors considered these species to be susceptible ; Bates regarded *M. opossum* as resistant. *M. nudicaudatus*, *C. philander*, *M. cinerea* and *M. incana* were susceptible. It is interesting that *C. philander* was susceptible to O.C. and Asibi strains, but not to J.Z. strain, showing that certain animal species may be resistant to one strain and fully susceptible to another strain indistinguishable immunologically from the first. This suggests that there may be still other yellow fever strains to which certain species of marsupials are more susceptible.

*J. F. Corson.*

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## DENGUE AND ALLIED FEVERS.

JOHNSON, J. A., Jr., MARTIN, W. B. & BRESLOW, L. **Dengue-like Fever on Okinawa.** *Bull. U.S. Army Med. Dept.* 1946, Mar., v. 5, No. 3, 306–11, 3 charts.

A short fever, in regard to which the authors state that " the diagnosis of dengue seems justified", made its appearance about the 7th April, 1945, among the U.S.A. troops in Okinawa Island [26°N. lat.]. The incidence increased gradually, reaching its peak in the middle of July, and then fell rapidly to zero about the middle of August. The rapid decline was associated with the establishment of mosquito control, which is said to have become good by the middle of July.

In April and May, the most abundant mosquito was *Culex quinquefasciatus* [*C. fatigans*]; *Aëdes albopictus* was rare, and "only occasional specimens" of *Aëdes aegypti* were found. In June and July, *Aë. albopictus* could readily be found, but *C. quinquefasciatus* was still the most prevalent mosquito; no further mention is made of *Aë. aegypti*. The epidemiological evidence was, therefore, somewhat against the diagnosis of "true dengue", but *Aë. albopictus*, despite its "low density", was thought to merit consideration as the possible vector.

The clinical aspects of the disease were regarded as differing from those of dengue in the relative infrequency of a secondary rise of temperature, the short average duration of the fever (3·04 days in a field hospital and 4·2 days in a "clearing company"), and the absence of a rash. In all other respects the disease conformed very closely to the generally accepted picture of dengue. In the field hospital, the percentage incidence of the chief symptoms and signs was as follows: Headache, 83; chill or chilliness, 92·5; orbital aches, 100; backache, 97·5; joint ache, 100; adenopathy, 85; conjunctivitis, 95; and leocopenia, 56·5. A definite reduction in the number of the polymorphonuclear leucocytes was observed by the 3rd or 4th day, when there was a relative, though not an absolute, lymphocytosis.

The maximum incidence of the disease in one infantry division, as shown in a chart, was at the rate of "275 per 1,000 per annum." Specimens of blood and serum have been submitted for virus studies.

[No reference is made to the occurrence of sandflies, so that presumably these were not in evidence. The clinical features are more suggestive of sandfly fever than of dengue.] *John W. D. Megaw.*

HÜHNE, W. Phlebotomen und Pappatacifieber in Nordkaukasien. (Referat ueber Arbeiten russischer Autoren u. eigene epidemiologische Beobachtungen.) [**Sandflies and Sandfly Fever in North Caucasia.**] *Deut. Tropenmed. Ztschr.* 1944, Apr.–May, v. 48, Nos. 7/10, 182–92. [22 refs.]

This paper consists almost entirely of a review of recent work by Russian observers on sandfly fever in the region north of the Caucasus Mountains, between the Sea of Azov and the Caspian Sea, where the author had personal experience of the disease in the summer of 1942. He had already seen cases of fever, clinically indistinguishable from sandfly fever, in the Don-Donetz region, situated further north where sandflies are not known to occur, so that the question arose whether the virus of sandfly fever was being transmitted by insects other than the sandfly, or whether the disease was caused by a different agency.

It was not till 1927 that sandflies, including *Phlebotomus papatasi*, were found to occur in Northern Caucasia; indeed so recently as 1934 an outbreak whose clinical features were those of sandfly fever was regarded as one of "mosquito disease". In 1935 widespread outbreaks occurred in the region and were attributed to virus transmitted by *P. papatasi*.

The disease was closely studied, especially by MOSCHKOWSKY and his colleagues, who in 1936–37 published a series of articles on the subject [see this *Bulletin*, 1937, v. 34, 856]. There seems to have been no important difference between the clinical features of the disease and those of sandfly fever in other countries.

In the summary of the experimental work by Russian observers, reference is made to successful immunization of human beings by injecting the virus after previous injections of convalescent serum, and to the passage of the virus through the eggs of experimentally infected sandflies to their offspring, and through the yolks of hens' eggs up to 48 passages.

References are given to 20 articles on the subject by Russian workers during the years 1936–1940. *John W. D. Megaw.*

NAJERA ANGULO, L. La fiebre de pappataci en España. [**Sandfly Fever in Spain.**] Reprinted from *Semana Med. Española.* 1946, Jan. 26, v. 9, No. 359, 87–98, 5 figs. [Bibliography.]

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## PLAGUE.

DEVIGNAT, R. Aspects de l'épidémiologie de la peste. [**Standardization of Epidemiological Surveys in Plague.**] *Bol. Oficina Sanitaria Panamericana.* 1945, Oct., v. 24, No. 10, 895–906, 1 chart & 1 fig. English summary.

In an introduction Dr. Devignat refers to the classical opinion originated by the Indian Plague Commission that the rôle of vector in plague, epidemic and epizootic, attaches to the flea *Xenopsylla cheopis*, and that subsidence of an epidemic is correlated with variation in the flea index. He cites exceptions and objections to this view and brings forward a scheme of standardization for the epidemiological study of plague which would apply to local conditions and yet be comparable with conditions prevailing elsewhere. He has applied his scheme to the study of plague, 1941–1943, in the region of Lake Albert in Belgian Congo. The scheme now proposed permits the inclusion of the *Rattus coucha ugandae* of Blukwa, with its infestation by *Xenopsylla* fleas, among the domestic rodents.

There are, according to Devignat, three fundamental plans of plague activity : the sylvatic and domestic murine plans and the human plan with six methods of possible contagion. These are intersylvatic, interdomestic, interhuman, sylvo-domestic, sylvo-human and domestico-human. He has devised a linear equation to determine Q the common index of epidemiogenic or epizootic transmissibility, based on modes of transmission. Various constants enter into the equation, such as K the constant of receptivity, k, k′, k″ . . constants of vection and variables in the shape of indices ; i, i′, i″ . . . rat flea indices and t, t′, t″ . . . flea-burrow indices. The technique for development of this standard scheme is given in detail. A chart is figured to show the application of the plan to Lake Albert. It may be noted that pulmonary plague is excluded from this suggestion of a standard plan to " summarize all the epidemiological aspects of plague in various countries." *W. F. Harvey.*

MACCHIAVELLO, A. Instrucciones para el diagnóstico, tratamiento y aislamiento de enfermos de peste bubónica, y para la recolección de muestras destinadas a exámenes de laboratorio. [**Instructions for Diagnosis, Treatment and Isolation of Plague Cases and for Laboratory Specimens.**] *Bol. Oficina Sanitaria Panamericana.* 1945, Aug., v. 24, No. 8, 704–12.

These instructions are set out in a series of 23 detailed and clear paragraphs. They should leave no practitioner, who is confronted with the possibility of plague, in any doubt what he should do. The first paragraph reads :—The present ordinance establishes the rules for diagnosis, isolation, and laboratory examination, including human autopsy, of bubonic plague as well as the simple examination required in every notification of certain or suspected human or rodent plague. The several instructions follow and the article ends with the printed form for cases of plague. *W. F. Harvey.*

WAYSON, N. E. & MCMAHON, Margaret C. **Plague : Treatment of Experimental Animals with Streptomycin, Sulfadiazine, and Sulfapyrazine.** *J. Lab. & Clin. Med.* 1946, Mar., v. 31, No. 3, 323–32, 1 fig.

Sulphonamide therapy has been extensively tested in plague, and the value of sulphadiazine has been established. The authors have now tested streptomycin, a product of *Actinomyces griseus* and, appropriately, controlled by comparison with sulphadiazine. Mice and guineapigs were the animals used, and infection was induced by inoculation and, also, in guineapigs more naturally through fleas. Streptomycin was given subcutaneously, dissolved in normal salt solution. Sulphonamides were suspended in acacia with double the dose of sodium bicarbonate, and administered orally by syringe or in capsules. This therapy was given after infection, and indicated that streptomycin had definite value. Summarizing, the authors say :—" (1) Three hundred and thirty-four white mice were inoculated with plague, and one-half were treated in groups with different amounts and varying dosage of either streptomycin, sulfadiazine or sulfapyrazine. The other one-half were used as controls. Under the treatment schedules finally adopted, from sixteen to eighteen survived among each lot of from eighteen to twenty, while all the corresponding controls died of plague. (2) Forty-eight guineapigs were likewise inoculated and one-half were treated with streptomycin in two groups after clinical evidence of infection had developed. All survived, but eight had residual buboes at necropsy. Twenty-three controls died with plague. (3) One hundred and six guineapigs were infected through flea transmission. After the disease was evident clinically, fifteen were treated with streptomycin and fourteen survived ; fifteen received sulfadiazine and fourteen survived ; ten received both these drugs and all survived ; sixteen received sulfapyrazine and ten survived. Six among all the survivors had residual buboes at necropsy. Three survived among fifty controls divided among the four lots treated. (4) Clinical recurrences appeared frequently under the treatment schedules used with streptomycin and sulfapyrazine, but not with sulfadiazine." *W. F. Harvey.*

KLINGENSMITH, C. W. **A Note on the Natural Occurrence of Fluoracetic Acid, the Acid of the New Rodenticide " 1080 ".** *Science*, 1945, Dec. 14, 622–3.

The sodium salt of monofluoracetic acid has recently been advocated as a rat poison [this *Bulletin*, 1946, v. 43, 331]. The acid itself has been shown by MARAIS (*Onderstepoort J. Vet. Sci.*, 1943, v. 18, 203–6 ; 1944, v. 20, 67–73) to be the toxic principle of *Dichapetalum* (=*Chailletia*) *cymosum*, called Gifblaar, a well known stock poison in South Africa. Another species in the genus *D. toxicaria* is a notorious poison in Sierra Leone, where it has been used by colonists for destroying rats. *R. B. Freeman.*

[MONSANTO CHEMICAL COMPANY]. **" 1080 " Rodenticide to be sold only to Pest Control Operators.** *Pests.* 1946, Jan., v. 14, No. 1, 28.

Owing to its very high toxicity, " 1080 " will not be on sale at any time to the general public. The lethal dose for man is believed to be " one-fiftieth of an ounce," about 8 mgm. per kgm. for a man of 60 kgm. (10 stone). No antidote is known. It is recommended for use at 0·04 per cent. on oats, one-fiftieth of an ounce to three pounds. Cases of deaths of dogs and pigs, presumed to be caused by eating poisoned rats, are recorded. Though not stated here, " 1080 " is sodium fluoracetate.

[A verbally identical note, except for statement about danger to domestic animals, occurs in *Chemurgic Digest*, 1946, Jan., v. 5, 22. There was an even briefer summary of the same press release in *Chem. Engng. News*, 1945, v. 23, 2367.] *R. B. Freeman.*

UPTON, R. G. **The Use of Antu as a Rodenticide.** *Pests.* 1945, Dec., v. 13, No. 12, 22.

Extensive field tests have been carried out with a-naphthylthiourea in Texas. It was mixed at 50 per cent. with 5 per cent. DDT and 45 per cent. inert powder, and dusted in burrows and runways; which method gave very poor results. The majority of the rats were *Rattus rattus alexandrinus*, which species is known to be much more resistant to this poison than *R. norvegicus*. It is very slow in action, deaths being recorded up to eight days. A considerable number of cats were killed. Chickens are said to be very resistant, a tenth of an ounce being required to kill a two-pound bird (nearly 3 grams per kilo.).

*R. B. Freeman.*

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## CHOLERA.

YACOB, M. & CHAUDHRI, J. R. **A Note on the Spread of Cholera Infection through Aerated Drinks.** *Indian Med. Gaz.* 1945, Dec., v. 80, No. 12, 634–6.

With the outbreak of epidemic cholera public health authorities tend to recommend or impose standard regulations as to food and drink upon the populace. Many of these regulations have been handed down for generations and have not been subjected to actual test. This certainly applies to aerated drinks and perhaps to ice. The authors have tested soda water and lemonade for their capacity to promote the growth of cultures of *V. cholerae* or, as the case may be, their vibriocidal action. These waters have a *p*H of 6·8 as compared with control water of 7·8, and the gas, which was not allowed to escape, had a pressure varying from 125 to 150 lb. For the ice experiments, water infected with cholera culture was converted to ice and was used after 24 hours to cool the aerated drinks. The conclusions are very interesting:—"The experiments described show conclusively that given sufficient time an aerated drink, even if infected with cholera, is rendered harmless by its own action." It is not certain whether the vibriocidal action is due to lowered *p*H, or to pressure of the gas, although, under the same experimental conditions, only one bottle out of five containing non-aerated lemonade gave a growth of cholera vibrios. "It also seems likely that cholera infected water, when converted into ice and served in drinks may also not prove harmful." *W. F. Harvey.*

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## BACILLARY DYSENTERY.

CHEEVER, F. S. **Dysentery Outbreak aboard Naval Vessels in San Pedro Bay, Philippine Islands.** *U.S. Nav. Med. Bull.* 1946, Apr., v. 46, No. 4, 479–94.

"During the months of July and August 1945 an outbreak of bacillary dysentery occurred on ships of the Third Fleet and Service Squadron 10 anchored in San Pedro Bay, Philippine Islands. More than 6,000 cases were reported during this period. The etiologic agent was Shigella flexneri III (VIII). The disease was clinically mild and only 3 deaths were recorded.

"The original focus of infection was apparently the native population. Naval personnel appeared to have become infected through contact with native food and drink, either ashore on the recreation beaches or afloat by patronizing bumboats. The subsequent inter-ship spread was probably caused by polluted

harbor water (small-boat personnel being particularly hard hit) and by personal contact between the crews of two or more ships that were tied up together. Once the disease became established aboard a crowded ship, it proved extremely infectious and hard to control in spite of the usual sanitary measures. Infected food handlers, convalescent carriers, and subclinical cases probably contributed to the spread of the disease. Flies may have been involved in the genesis of the epidemic on the beach, but they played no role in the subsequent spread of the disease in the anchorage. No evidence was disclosed that fresh water obtained by distillation of harbor water was contaminated, and the epidemiologic picture was not one of massive water-borne infection.

"Experimentally it was proved that strains of the specific organism recovered comparatively late in the epidemic could survive at least 2 days in sea water, and that they were relatively resistant to the bacteriostatic action of sulfadiazine and sulfathiazole. This property of drug fastness is one explanation for the noteworthy failure of chemoprophylaxis to check the epidemic."

MOORE, F. J., KESSEL, J. F., SIMONSEN, D. G. & MARMORSTON, Jessie, with the technical assistance of H. LLEWELLYN, F. KAPLAN, F. GOLDEN, N. ANDERSON & E. JAFFE. **Experimental Basis of Sulfonamide Therapy in Bacillary Dysentery.** *J. Infect. Dis.* 1946, Jan.–Feb., v. 78, No. 1, 25–31. [26 refs.]

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## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

BROWN, A. G. **Experiences with Amoebiasis in an Evacuation Hospital.** *War Medicine.* Chicago. 1945, Nov.–Dec., v. 8, No. 5, 319–24.

In a 400-bed American Evacuation Hospital, during two years' service in North Africa and in Europe, intestinal amoebiasis was diagnosed in 243 patients and hospital personnel. The majority of these had been hospitalized for gastro-intestinal symptoms. A survey of the hospital personnel, after 18 members had been treated for acute amoebic dysentery, showed that 65 of 298 (21·8 per cent.) were infected with *Entamoeba histolytica.* Diagnosis was at first made in the usual manner by the examination of fresh specimens of stool. Subsequently, Schaudinn-fixed smears were stained with iron-alum-haematoxylin, as difficulty was experienced in identifying cysts and "precysts" in fresh preparations. A rapid method of fixation and staining, taking little more than one hour is described.

Treatment, where undertaken, was daily for 10 days with emetine injections, accompanied, and followed after a week's interval, by courses of carbarsone or chiniofon, as recommended by U.S. Army Headquarters, North Africa. One week after completion of the second course, three stools were checked. "In only 1 case were Endamoeba histolytica cysts still present after the two courses, and this patient was evacuated for further therapy. In a few cases amebas other than Endamoeba histolytica were not all destroyed by the course of therapy."

[The difficulty experienced generally by service pathologists in differentiating the morphologically characteristic cysts of the intestinal protozoa in fresh unstained preparations of faeces is perhaps not unduly hard to understand. But the ease with which these pathologists can specifically identify, in fresh preparations and after a saline purge, the much less obviously characteristic vegetative stages of these same parasites is more difficult to grasp. The postulate "it moves—it's an amoeba; it has engorged red cells—it's *histolytica*" is possibly reasonably accurate for the detection of the acute amoebic dysenteric, but it cannot be regarded as adequate for the purpose of a survey of

infection rates. This does appear to have been recognized to some extent in the study recorded in the present paper, as staining methods after fixation were adopted.] *A. R. D. Adams.*

LUCAS, R. B. **Culture Methods in the Diagnosis of Amoebiasis.** *J. Roy. Army Med. Corps.* 1945, Nov., v. 85, No. 5, 249–51.

Using Loeffler's serum slopes covered with Ringer's solution to which egg albumin and rice starch were added, the author attempted to cultivate *E. histolytica* from the faeces of 405 patients sent to the laboratory of a military hospital in an area in which amoebiasis was endemic. *E. histolytica* was discovered in 18 by direct microscopical examination, and all these gave a positive culture. In addition, positive cultures were obtained in 24 cases in which amoebae were not discovered by the microscope. It is concluded that culture of faeces for *E. histolytica*, as a routine measure, can be of considerable value in the diagnosis of amoebiasis. *C. M. Wenyon.*

LAWLESS, D. K. **Detecting Intestinal Protozoa. Saline-Iron-Hematoxylin Solution for Wet Smears.** *Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 133–4.

Cysts and trophozoites of intestinal protozoa in faeces are easily distinguished from similar objects and from the background if fresh slide preparations are made with the following mixture: normal salt solution, 75 cc.; 0·5 per cent. haematoxylin solution, 10–15 cc.; 4 per cent. ferric ammonium sulphate, 0·25 cc. A small particle of faeces is emulsified in a drop of the solution to make a thin film under a coverslip; the protozoa are seen against a black-stained background. *J. F. Corson.*

HAMZAH, N. A. **Amoebic Appendicitis.** *J. Palestine Arab Med. Ass.* 1946, Mar., v. 1, No. 3, 72–4.

Of 50 appendices removed consecutively at the Government Hospital, Haifa, Palestine, 13 had amoebic ulcers (amoebae present), 9 had other ulcers, 21 had "diffuse infiltration", and 7 had worms; 4 were gangrenous, but none of these was amoebic.

In 12 of the 13 cases with amoebic ulcers the appendix appeared normal or slightly thickened externally, and the mucosa looked normal except for two or three greyish sanguineous sloughs covering ulcers with undermined edges; the ulcers were mostly limited to the mucosa, but in a few cases they extended to the serous coat.

These 13 cases were diagnosed before operation as subacute appendicitis; they had a history of slight pain in the right lower abdominal quadrant for months or even years, and tenderness over McBurney's point was present in all.

The author concludes that from 20 to 30 per cent. of cases of subacute or chronic appendicitis in Palestine are of amoebic origin. If amoebae are found in the stools before operation, medical treatment should first be given and operation should be done later to prevent relapse. *J. F. Corson.*

GOLDEN, R. & DUCHARME, P. **The Clinical Significance of Deformity of the Cecum in Amebiasis.** *Radiology.* 1945, Dec., v. 45, No. 6, 565–80, 6 figs [14 refs.]

Amoebiasis is common in the United States, and its diagnosis may be difficult. Sixty-seven patients (in 58 of whom *E. histolytica* was recognized in the stools, and in 9 of whom this organism was assumed to be present though not actually found) were radiographed after a barium meal (27), or after a barium enema (18)

or after both (22). Thirty-three of the 67 patients suffered from diarrhoea, 9 complained of various abdominal symptoms, but not of diarrhoea ; and the remaining 25 were either free from abdominal symptoms (18), or there was inadequate information in respect of these (7). In 30 of the 67, including 18 of those complaining of diarrhoea, and 21 of the microscopically proven cases of amoebiasis, deformity of the caecum was observed radiographically. This deformity varied considerably : in some cases it was slight and consisted of narrowing of the tip ; in others the caecum was markedly shrunken, but its outline was generally smooth and only rarely irregular. Where deformity occurred there was usually localized tenderness over the caecal area, and in some cases pressure apparently accentuated the deformity. In no case was narrowing or intrinsic deformity of the terminal ileum seen, although in one instance obliteration of the folds and the smoothness of the shadow suggested oedema of the ileal mucosa. This cleared after specific anti-amoebic treatment.

Five patients with caecal deformity were re-examined after treatment. In four there was " relaxation of the caecum " suggesting improvement. In the fifth case, with a markedly shrunken caecum, there was no change. From this the authors deduce that the caecal changes produced by amoebiasis in its later stages are irreversible. They conclude that caecal deformity, demonstrable on radiography, is likely to be seen in over one-third of cases of amoebiasis, more particularly in those with intestinal symptoms ; it may give a valuable pointer to the diagnosis, but its absence does not exclude a diagnosis of amoebiasis.

*A. R. D. Adams.*

ISAAC, F. **Roentgen Findings in Amebic Disease of the Liver.** *Radiology.* 1945, Dec., v. 45, No. 6, 581–7, 5 figs.

Amoebic involvement of the liver is the most common complication of amoebic dysentery. It is more common in visitors to the tropics than in the Natives. Of 222 cases of amoebic dysentery in an Army Hospital overseas 32 (14 per cent.) suffered embolic liver infection. Two stages of liver trouble were seen, a diffuse hepatitis (without jaundice) and, later, amoebic abscess or multiple abscesses. Clinical differentiation of the stages is difficult unless aspiration or drainage is done. These are rarely necessary if early specific treatment is instituted, and so most of the author's cases were designated amoebic hepatitis. On X-ray examination about half his patients showed no signs, or, at most, downward enlargement of the liver. These were probably cases of diffuse amoebic hepatitis. The other half showed doming of the right diaphragm, with flattening of the costophrenic sinus. The doming may be restricted to the outer portion of the diaphragm ; or it may be in the mesial portion, and the cardiophrenic angle is then obliterated. Sometimes the elevation is limited to the middle portion of the right diaphragm, and the costophrenic and cardiophrenic angles are sharpened. Elevation of the right diaphragm is the most unequivocal sign of amoebic liver abscess. On screening, limitation of movement with sluggishness or fixation of the right diaphragm may be seen. The right lower lung field may show changes resembling an atypical primary pneumonia, owing to compression of the base by the raised diaphragm, or to an interstitial pneumonitis or to partial atelectasis. There may be a pleural reaction with thickening of the pleura and effusion into the costophrenic sulcus. This probably arises from rupture of the liver abscess into the right pleura, and the chest signs may then mask the causative liver lesion.

Most cases of amoebic liver disease respond to medication without operative interference or aspiration. Illustrative cases are cited, with reproductions of radiographs.

[No mention is made of the possibility of variation in the site of amoebic abscesses in the liver. It is apparently assumed that these *always* occur in the upper portion of the right lobe.] *A. R. D. Adams.*

COTTRELL, J. D. & HAYWARD, G. W. **The Effects of Emetine on the Heart.** *Brit. Heart J.* 1945, Oct., v. 7, No. 4, 168–70, 2 figs.

"Changes in the electrocardiogram, blood pressure, and pulse rate produced by emetine and emetine bismuth iodide have been studied in soldiers under treatment for amoebiasis. All were otherwise healthy and the initial cardiograms were normal. Diminution or inversion of the T waves occurred in one or more leads in 25 out of 32 cases receiving emetine and in 12 cases there was an increase in the P-R interval of from 0·02 to 0·04 sec. Similar changes occurred during treatment with emetine bismuth iodide, 7 out of 8 cases showing diminution in T waves and prolongation of the P-R interval. The cardiogram returned to normal 8–12 days after the completion of treatment. The effect on the blood pressure and pulse rate of both drugs was insignificant, and in no case was there any clinical evidence of myocardial insufficiency."

BERBERIAN, D. A. **Treatment of Lambliasis with Acranil.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 441–4. [27 refs.]

The author has treated 50 cases of giardia infection in children with Acranil [see this *Bulletin*, 1945, v. 42, 909]. The dose of the drug varied around 0·1 gm. twice or thrice daily for five days. In some cases an initial dose of 0·2 gm. to 0·5 gm. commenced the course. Following the treatment, five weekly examinations for giardia infection were carried out. It appeared that in all the 50 children, as well as in three adults, Acranil had eradicated the infection. It is noteworthy that other protozoal and helminthic infections were unaffected by the drug, which was well tolerated by all the children, though a slight coloration of the skin occurred. *C. M. Wenyon.*

## RELAPSING FEVER AND OTHER SPIROCHAETOSES.

ADVIER. La fièvre récurrente et ses accidents nerveux. [**Relapsing Fever and its Nervous Manifestations.**] *Les Grandes Endémies Tropicales.* (Onzième Année.) 1939. Paris. pp. 33–48.

A useful summary of the history of relapsing fever, with special reference to the occurrence of the disease in the French Colonies. The title of the article, however, is somewhat misleading since little more than two pages are concerned with relapsing fever as it affects the nervous system. *E. Hindle.*

MOLLARET, P. & DIGO, R. Association probable d'une pasteurellose et d'un biokoshio (sodoku par morsure de chat). [**Probable Association of a *Pasteurella* Infection with Cat-Bite Fever.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 3, 4, 5, 6 & 7, 137–40, 1 fig. [18 refs.]

## LEPROSY.

NEWMAN, P. P. **A Visit to an Indian Leper Colony.** *Brit. Med. J.* 1946, Apr. 20, 616.

PRABHU, M. N. **Leprosy of the Upper Respiratory Passages.** *Leprosy in India.* 1946, Jan., v. 18, No. 1, 10–12.

The author, who was resident medical officer in charge of ear, nose and throat hospital cases at a Madras hospital, reports the results of examinations

carried out at the Silver Jubilee Leprosy Clinic, including bacteriological examinations, during a period of six months. The evidence indicates that nasal infections are the result of general rather than of local infections. In simple macular neural leprosy the nose is seldom, if ever, infected, but in major tuberculoid leprosy, nasal lesions are not uncommon. The nasal mucous membrane first becomes congested and oedematous, with greyish, whitish or yellow inflammatory spots, and it bleeds easily. Lepra bacilli can be found in small numbers only, and blocking of the nose results with the formation of crusts. Later, ulceration occurs ; the septum may be perforated and destruction of cartilages, with deformities, may result. The mouth, tongue and pharynx may become involved in advanced lepromatous disease, and perforations of the hard or soft palate may resemble those due to syphilis. Nodules occur, and also leprous glossitis, which may be extremely painful. In such cases the larynx may become similarly affected, first with thickening of the epiglottis, with spread to the vocal cords, either as an ulcerative or a fibrotic condition. Much swelling and oedema may necessitate tracheotomy.

*L. Rogers.*

MUIR, E. **Elephantiasis and Septic Infection.** *J. Trop. Med. & Hyg.* 1945, Dec.–1946, Jan., v. 48, No. 6, 145–8, 3 figs.

In this paper a comparison is made between lepromatous leprosy and filarial elephantiasis as regards secondary septic infection and the development of pachydermatous conditions ; in both cases associated with lymphatic obstruction and with periodic inflammatory changes. In the filarial disease the febrile attacks are associated with monthly parturition of the adult female worms, with the production of very large numbers of embryos, as shown by ROGERS, and are accompanied by lymphangitis, which may be of septic origin. Allergy is also thought to play a part in this process. In lepromatous leprosy the frequent febrile reactions may similarly be caused by secondary septic organisms, by blocking of small lymphatic vessels, and by allergic reactions like those produced by the injections of protein matter derived from lepra bacilli, such as followed the use of Dharmendra's lepromin, or by the administration of iodides, as shown by Muir himself. An illustration is given which shows great swelling of the face during an acute lepra reaction, and another shows a pachydermatous condition of the face. Attempts to control lepra reactions by sulphonamide drugs failed, but more recently promin and diasone, which inhibit the growth of the tubercle bacillus, have proved more effective, especially in inflamed eyes and ulcerated noses. Soluseptasine given intramuscularly cleanses septic leprotic ulcers rapidly ; the action of penicillin resembles that of diasone and promin in advanced lepromatous cases, and as penicillin is inert against tubercle bacilli, and probably against *Myco. leprae*, the action of all three is probably on the septic infection. All this points to septic infections playing an important part in the causation of lepra reactions.

*L. Rogers.*

WEEKS, K. D. & SMITH, D. T. **Lepromin Skin Tests in Boeck's Sarcoid.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 519–21, 1 fig.

This brief note records lepromin tests in ten cases of Boeck's sarcoid, including several previously reported by HARRELL. The clinical symptoms were typical in all and were confirmed by microscopical examinations. In seven the lepromin test was negative and six of these were also negative to tuberculin. In the remaining three, lepromin gave positive reactions and in two of them tuberculin also gave positive results. Two cases of active tuberculosis gave positive lepromin tests. No evidence was obtained that Boeck's sarcoid is an attenuated or modified form of leprosy.

*L. Rogers.*

HARRELL, G. T. & HORNE, S. F. **The Reaction to Lepromin of Patients with Sarcoid or Tuberculosis compared with that of Patients in General Hospitals with a Discussion of the Mechanism of the Reaction.** *Amer. J. Trop. Med.* 1945, Nov., v. 25, No. 6, 523–35, 7 figs. [17 refs.]

This paper also deals with lepromin tests to determine if Boeck's sarcoid may be caused by the *Myco. leprae*, as suggested by the clinical and pathological resemblances between certain cases of sarcoid and tuberculoid leprosy. It deals with 70 patients tested with lepromin ; they included 5 with sarcoid, 5 with active tuberculosis, 41 with healed or inactive tuberculosis, who were suffering from a variety of chronic diseases, and 18 with a variety of acute and chronic diseases. The authors regard early erythematous reaction with lepromin as less specific than the later infiltration and ulceration which occurs at the site of the lepromin injection in positive cases. Full details of the tests are given, and the results tabulated ; from a study of these, the authors come to the following conclusions. In patients with sarcoid the reactions are slight and infrequent ; they give no indication that sarcoid is atypical tuberculoid leprosy. In a control group in the U.S.A. the incidence of intense or moderately intense lepromin reactions is less than in endemic areas of leprosy in the tropics. The high incidence of strong late lepromin reactions in active tuberculosis suggests the presence of common sensitizing antigens, possibly soluble protein or polysaccharide. It is also suggested that a lipid may be the active chemical fraction. If tuberculosis can be ruled out, lepromin may prove useful in the diagnosis, as well as the prognosis, of leprosy. The authors suggest that leprosy, like tuberculosis, may be a disease of high contagion, slow progression, and high curability, requiring repeated regular exposures to the infecting organism. Attempts should therefore be made by frequent inoculations of living organisms into animals, over a long period, with a view to their infection. As the living monocyte appears to furnish a substance essential for the growth of the *Mycobacterium leprae*, attempts should be made to cultivate it by the inoculation of tissue cultures of monocytes, or of chick egg chorio-allantoic membrane, with infected material. *L. Rogers.*

CORRECTION.

Professor DE SOUZA-ARAUJO has called attention to the fact that, for the experiments referred to in the abstract in this *Bulletin*, 1945, v. 42, 1010, he used his original cultures of acid-fast bacilli isolated from leprosy material, and not emulsions of material rich in Hansen's bacilli, as stated in the abstract.—*Ed.*

SLOAN, T. B. M. **The Rôle of Propaganda in the Control of Leprosy.** *Leprosy in India.* 1946, Jan., v. 18, No. 1, 15–22.

The subject is dealt with on very general lines, with special emphasis on education of the public. The author thinks that too much attention is being paid in India to treatment, rather than to isolation of infective cases. Legislation is not needed for the control of patients with neural leprosy, but more persuasion is required for the isolation of lepromatous cases. Propaganda should be prepared by a professional publicist, and radio talks and discussions should be arranged. Posters and slogans should be displayed in schools and public buildings so as to combat common prejudices among the illiterate. The author supports the view that the word " leper " should not be used. School teachers should be instructed on the subject as well as employers of labour, who should know that 75 per cent. of all cases are uninfective. *L. Rogers.*

BLOSS, J. F. E. **The Control of Leprosy among the Azande, Anglo-Egyptian Sudan.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 423–36, 1 map.

This valuable report brings up-to-date information on work for the control of leprosy in the heavily infected, humid southern Sudan, where much leprosy was discovered during operations against an outbreak of sleeping sickness. Dr. ATKEY, the P.M.O., originally ordered a leprosy survey, which was carried out by Dr. CRUICKSHANK in 1929, with the discovery of 6,400 cases within two years, representing 3·3 per cent. of the population, whose diet was deficient in animal proteins. In 1929–30 a total of 5,500 lepers—some 80 per cent. of the known cases in the district—were transferred with their families to two large settlements, at Souras Yubu and Li Rangu, and treated, mainly by Alepol intravenously, which was found to be the most effective preparation. By the end of 1931, 30 per cent. of the patients had improved, and 40 per cent. more were discharged as quiescent and uninfective. Advanced lepromatous cases were now segregated in special camps to diminish the chances of infection. In 1935, WOODMAN (*Sudan Med. Serv. Ann. Rep.*, 1935) estimated the disease incidence at 7 per cent. of the population, and reported that the records of 3,500 cases [see this *Bulletin*, 1938, v. 35, 295] showed good results from treatment with chaulmoogra derivatives for periods not exceeding 3 or 4 years, after which no further benefit accrued. He considered that the Li Rangu settlement, with 25 sq. miles of land, then the largest in Africa, was of value in isolating the most infective cases and in facilitating treatment. In 1935 the Li Rangu settlement figures were :—

| | |
|---|---|
| Advanced cases segregated ... ... ... ... ... ... | 204 |
| Under observation or treatment in settlement ... ... ... | 1,021 |
| Discharged cases, cures and quiescent, living in settlement ... | 951 |
| Discharged cases living outside settlement ... ... ... ... | 513 |
| Total ... ... ... ... ... ... ... ... | 2,689 |
| [Total cured or quiescent (951+513) ... 1,464 (54·4%)] | |
| Outside cases which had never been in the Settlement ... ... | 809 |
| Total ... ... | 3,498 |

This settlement, however, was overcrowded.

In 1939–40 a new survey and census was made, and yearly inspection of the whole population was being carried out ; in 1941 a card index overcame difficulties in registration of patients. The total known cases had fallen to 1,955, and the new cases had declined from 283 in 1939 to 186 in 1941 and 86 in 1942.

Conditions in the settlement have now been improved, and agricultural work is paid for ; this furnished almost all the food crops for much increased rations. During the war Alepol supplies ran out, and treatment has been disappointing. The age incidence now shows that less than 12 per cent. of the known cases are in persons under 20 years of age, against 21 per cent. in 1930. " This points to (*a*) the disease being under control, and (*b*) that a decrease rather than an increase in the number of cases is to be expected in the future." A gradual decentralization is now being aimed at by organizing a number of local, small, chief's colonies in place of one very large settlement, coupled with an increase in public health activities and improvement in the standards of living.

*L. Rogers.*

CHANDY, P. J. **The Problem of the Discharged Patient.** *Leprosy in India.* 1946, Jan., v. 18, No. 1, 13–14.

This is a short note by the medical officer of the Fyzabad Leper Home and Hospital, which deals with 40 cases discharged during the previous six years.

Patients with arrested disease are often unwilling to leave the institution to make room for more suitable patients, on account of social prejudices and difficulty in obtaining employment under favourable living conditions. Eight of the 40 discharged cases had relapsed, not a very high rate, but enough to make an employer loath to run any risk. Discharged patients may meet with difficulties in returning to live in their own villages ; patients who show any deformity are especially viewed with suspicion. Two developed tuberculosis, which is common among leprosy patients. A few can be employed after recovery in leprosy institutions. The author suggests that industrial and agricultural settlements should be started near each leprosy institution, which will ultimately become self-supporting, and provide the best solution of the problem. *L. Rogers.*

PRUDHOMME, R. O. Conservation de la vitalité du bacille de Stéfansky dans des lépromes desséchés. [**Conservation of the Vitality of Stéfansky's Bacilli.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 11/12, 338–44.

MARCHOUX and SOREL (*Ann. Inst. Pasteur*, 1912, p. 1) have shown that when Stéfansky's bacilli of rat leprosy are dried for two days over sulphuric acid in a vacuum, they are no longer infective to rats, and that they also die when preserved for 15 days at 37°C. in physiological saline. The vitality of the organisms can be tested without animal inoculation if to 1 cc. of a pure emulsion of the bacillus is added 1/20 cc. of a solution of orthocresol-indo-2-6 dichlorophenol, N/10,000 in boiled distilled water, and the blue mixture is placed in an ampoule which is sealed after removal of the contained air. If the bacilli are living at the end of 24 hours the contents of the ampoule will have become decolourized, but not if they are dead. By the use of this test and by the inoculation of rats the authors have found that bacilli contained in a leproma, frozen and crushed at —28°C. and then dried and kept in a vacuum at from 0° to 4°C., retained their virulence for rats for over one year ; but if kept in the presence of air they died. Lepromata dried over sulphuric acid also kept their virulence for over a year in a vacuum, but not in air. *L. Rogers.*

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## HELMINTHIASIS.

TARR, L. **Effect of the Antimony Compounds, Fuadin and Tartar Emetic, on the Electrocardiogram. A Preliminary Report.** *Bull. U.S. Army Med. Dept.* 1946, Mar., v. 5, No. 3, 336–9, 1 fig.

Electrocardiograms were taken in 150 patients who had returned from abroad where they had suffered from schistosomiasis and had been treated with Fuadin or tartar emetic or both, at times varying from 22 to 112 days previously. They showed no clinical symptoms or signs of organic heart disease and all except four of the electrocardiographic tracings were normal. In 66 patients, ova of *Schistosoma japonicum* were present in the faeces and the patients were given further treatment with antimony ; electrocardiograms were taken under standard conditions before, during, and after this treatment.

Fuadin—intramuscular injections every other day of a 6 per cent. solution to a total of 65 cc. (0·566 gm. of antimony) in 14 injections—was given to 28 patients, while tartar emetic—intravenous injections every other day of 0·5 per cent. solution to a total of 320 cc. (0·576 gm. of antimony) in 15 injections —was given to the other 38 patients.

The only change in the electrocardiogram was a decrease in the voltage of the T wave, of different degrees which the author classifies as one plus, two plus,

three plus, and four plus, respectively, only the last two being significantly different from normal tracings ; these, however, might easily have been interpreted as indicating myocardial damage or even coronary occlusion. The three plus or four plus changes occurred in 12 (31 per cent.) of the 38 patients treated with tartar emetic and in only two of the 28 who were treated with Fuadin. There was no apparent relationship between the maximum changes in the electrocardiogram and toxic effects of the drugs and in no case was the course of treatment altered because of such changes. The return to a normal cardiogram began some days after the end of treatment and was usually complete within a month.

The author regards the electrocardiographic change as a transient reversible effect of trivalent antimony on the heart and its only importance is the possibility of mistaking it for serious myocardial damage. [The author somewhat misrepresents the findings of MAINZER and KRAUSE (this *Bulletin*, 1940, v. 37, 487) ; in 7 of their 12 cases the electrocardiogram showed either a " definitely pathological tracing during the antimony treatment " (3 cases) or a curve which " suggests the suspicion of an altered function of the cardiac muscle " (4 cases).] *J. F. Corson.*

TORRES, C. M. & PINTO, C. Mecanismo de eliminação dos ovos de *Schistosoma mansoni* estudado no tatù (*Euphractus sexcinctus*). [**Mechanism of Elimination of the Eggs of** *S. mansoni* **in the Armadillo.**] *An. Acad. Brasileira de Ciencias.* 1945, Dec. 31, v. 17, No. 4, 271–2, 2 figs. on pls.

The armadillo to which the authors refer died 94 days after infection, and at autopsy 86 female and 23 male *S. mansoni* were found in the liver, and two of each sex in the pancreas. In the walls of both small and large intestine there were numerous granulomata and eggs, but there were interesting differences, in the distribution of the lesions, between the small and the large intestine. In the small intestine, granulomata and eggs were always localized in the submucosa, never above the muscularis mucosae ; the small intestine is evidently not the route by which eggs are passed to the exterior. In the large intestine, on the other hand, the granulomata and eggs are most numerous in the mucosa itself, and are rarely seen in the submucosa. Elimination of eggs into the faeces is therefore exclusively performed in the large intestine.

The mechanism of elimination is complex. It depends on various factors :—(1) the structure of the intestinal wall and its vessels ; (2) the extrusion of the eggs from the capillaries, and their fixation in the mucous coat at the level of the fundi of the crypts of Lieberkühn ; (3) the formation of cellular infiltration round the eggs ; (4) histolysis of the walls of the crypts, by products elaborated by the eggs ; (5) elimination to the exterior along with the intestinal secretions. The important part of this process is the elaboration of histolytic substances by the embryo. In the large intestine the authors found cystic dilatation and hypertrophy of the glands, which may have been the precursors of adenomatous polypi. *Charles Wilcocks.*

HILLEMAND, P., VARAY, A., DEBRAY, J. R. & DUGUET, Mme. A propos d'un cas de distomatose hépatique. [**A Case of** *Fasciola hepatica* **Infection.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 1/2, 50–52.

The patient, a man aged 30, was first treated in August 1942 for irregular vomiting and diarrhoea, without benefit ; in January 1943 he was again examined and the diagnosis of infestation with *Fasciola hepatica* was suggested by blood examination which showed 67 per cent. of eosinophiles, and was confirmed by finding the ova in the faeces.

He developed pleural effusion at this time, associated with fever (40°C.) on the first day but the temperature fell to 38°C. next day before treatment with sulphonamides was begun, and became normal a few days later. Lymphocytes formed 70 per cent. of the cells of the pleural fluid and culture of the fluid remained sterile. The effusion meanwhile disappeared without any apparent involvement of the lung.

A week later (7th February) treatment with emetine was begun ; seven injections of 8 cgm. [1¼ grain] were ordered but by a mistake a single dose of 40 cgm. [6 grains] was injected and caused no untoward symptoms. Altogether he got 80 cgm. of emetine. Improvement was rapid, the eosinophilia decreased to 31 per cent. in a few days and his weight increased by 2 kgm.

Six months later (August) treatment with stovarsol was begun [no mention is made of faecal examination] and the eosinophilia decreased to 8 per cent., and in January 1944 it was 5 per cent. He was then given another course of emetine injections and recovered completely.

The author suggests that the pleural effusion was a pleural form of Loeffler's syndrome. The rapid improvement after the first course of emetine leads him to think that it might have been due to the large dose of emetine given by mistake. [For other references to infestation of man with *Fasciola hepatica*, see this *Bulletin*, 1942, v. 39, 14, 703 ; 1943, v. 40, 253, 472 ; 1944, v. 41, 677, 1052.] *J. F. Corson.*

EDWARDS, C. **Cerebral Cysticercosis without Epilepsy.** *Lancet.* 1946, Apr. 6, 500–501, 1 fig. on pl.

An airman, aged 42, was invalided to England from the Azores, after 5 months' service, in July 1944 because of two attacks of aphasia, one in May and the other in June of that year. He had lived in the Middle and Far East from 1919 to 1925 and had since lived in England. In 1937 he developed a "vague" frontal headache which had been almost constantly present ever since. In 1942 he awoke one morning to find that the left half of his field of vision was impaired and this has since remained unchanged.

Medical examination in July 1944 showed "incongruous homonymous hemianopic defects involving chiefly the lower left quadrant." No abnormality was seen by radiography of the skull. Lumbar puncture was done and the cerebrospinal fluid showed a pressure of 90–100 mm. of water and normal Queckenstedt test ; there were : no cells, protein 0·07 per cent., a very slight increase in globulin, negative Wassermann reaction, and the Lange gold curve was 443321000. The blood also gave a negative W.R. ; there were 8,300 white blood corpuscles, and a differential count showed polymorphonuclears 60 per cent., lymphocytes 35 per cent., eosinophils 3 per cent., and monocytes 2 per cent.

On the 4th day after the lumbar puncture an irritable rash appeared on the thighs, legs, elbows and forearms and lasted for about 4 days.

On suspicion of a neoplasm being present the chest was radiographed and this disclosed the presence of numerous small calcified bodies in the muscles and subcutaneous tissues which were seen also all over the body. They were obviously cysticerci and careful search showed two subcutaneous nodules in the epigastric region and one in the left upper arm. An encephalogram was taken and showed "short runs of waves with a frequency of 22 per sec. in both parietal regions. These interrupted a stable dominant frequency of 10 per sec. The disturbances which were numerous were considered to be epileptic in type." The patient was invalided from the Service, his only symptom then being a slight headache.

The author notes that the incubation period (at least 12 years) is one of the longest recorded; DIXON and HARGREAVES [this *Bulletin*, 1945, v. 42, 907] reported one of 20 years. Reference is also made to papers by MAC ARTHUR [this *Bulletin*, 1934, v. 31, 384] and MARSH [*ibid.* 786; see also ELSAESSER, *ibid.*, 1946, v. 43, 228]. *J. F. Corson.*

DICK, G. W. A. & MCCARTHY, D. D. **The Absence of Anaemia in Hookworm Infestation in East African Personnel.** *East African Med. J.* 1946, Jan., v. 23, No. 1, 19–22. [13 refs.]

McCarthy [this *Bulletin*, 1931, v. 28, 21] made observations on natives in Pemba Island who had severe anaemia associated with hookworm infestation; the more heavily infested patients were treated with oil of chenopodium, iron and arsenic, as well as being given a full diet, while the less heavily infested patients were given a full diet, extra eggs and fruit, and 1·5 gm. of marmite daily, but received no drugs. He concluded that the cause of anaemia associated with hookworm infestation was "an inadequate and probably deficient diet."

Dick made observations, recorded in the present paper, on 67 East African native soldiers in whose faeces hookworm ova were the only indication of the presence of pathogenic parasites (*Strongyloides stercoralis* and *Trichuris trichiura* were regarded as non-pathogenic). The controls were native soldiers with no evidence of any intestinal infestation. The observations consisted of erythrocyte counts and estimations of haemoglobin in the blood. The average number of erythrocytes (4·9 millions per cmm.) was the same for the patients and the controls and the average haemoglobin content was slightly higher in the patients (101 per cent. or about 17 gm. per 100 cc.) than in the controls (99 per cent.).

The authors discuss the significance of their observations and conclude that hookworm infestation, unless it is very heavy, does not cause anaemia in East African natives who are well fed and are living under good conditions; when anaemia occurs it is due partly to deficiency of blood-building material (protein and iron) in the diet and partly to removal of blood by the hookworms. In such cases a good diet is more important than anthelmintics. *J. F. Corson.*

CRUZ, W. O. & DE MELLO, R. P. Profilaxia da anemia ancilostomótica Sindrome de carencia. [**Hookworm Anaemia a Food-Deficiency Syndrome. Its Prophylaxis.**] *Mem. Inst. Oswaldo Cruz.* 1945, Apr., v. 42, No. 2, 401–48, 11 graphs. [19 refs.] English summary.

[An account of an interesting series of experiments.] The fact has been observed that severe anaemia associated with ankylostomiasis occurs mainly in patients on a qualitatively insufficient diet; also that iron in the proper doses will cure the anaemia even though the worms persist. Further, those who suffer from deficiency of iron in their diet are the ones to develop severe anaemia when they become infested with hookworm. On these grounds the suggestion is made to apply the administration of Fe salts in food, prophylactically, against hookworm anaemia, analogous to the use of iodide in the prevention of goitre. Hitherto, the prophylaxis of ankylostomiasis and its associated anaemia has been attained by treatment of patients and the provision and use of latrines.

The end which the authors had in view was more difficult of attainment than the giving of iodide salt for goitre, for several reasons. Thus, the salt of Fe, though in considerable quantity, must not be such as to make the food unpalatable; the salt must remain stable for the time elapsing between mixing

with the food and partaking of the meal; the colour of the food must not be so changed that contamination would be suspected; the salt used ought to be haematologically active in small doses and it should be cheap and easily obtainable.

The authors tried 12 different salts of Fe; the carbonate, phosphate, glycerophosphate, the sulphate, the scale preparations and others, added them to cooking-salt, to sugar, to flour or meal, noted the colour of the mixture, the taste, and the effect of therapeutic doses on the blood. The best was found to be ferrous sulphate mixed with meal or cooking-salt, and with the latter of these there was considerable taste detectable, so that the most efficient of all was the mixture with flour of manioc, or cassava meal. Another good mixture was Ferri et ammon. cit. with baked beans, but this was more difficult in practice because the mixture changed the colour and it had to be very carefully prepared.

The dosage was usually Ferri sulph., 1 gm. daily, till the haemoglobin reached the normal level of 10–11 gm. per cent., the therapeutic period; then half this dose, 0·5 gm. daily for some 80 days, and after that 0·25 gm. for a like period; the haemoglobin was thus maintained. Then a vermifuge was given, 3 doses in 26–30 days, or 4 doses in 40 days or so and the numbers of worms passed were counted. They might amount to several hundreds (717 in one case). Individual results are presented in graphs and tables.

*H. Harold Scott.*

YANG, S. C. H. & LAUBE, P. J. **Biliary Ascariasis. Report of 19 Cases.** *Ann. Surgery.* 1946, Feb., v. 123, No. 2, 299–303.

The authors review some of the literature which records the high incidence of ascariasis in man in China and elsewhere, yet the importance of biliary ascariasis is not sufficiently realized. MUIR [this *Bulletin*, 1932, v. 29, 752] reported on a Chinese subject who had an ascarid in the common bile duct, and he quotes 90 cases collected by AVILES [*Surg., Gynecol. & Obstet.*, 1918, Nov., 459] from the literature up to 1918, and also 12 cases of biliary ascariasis detected at autopsy in the Philippine Islands. MORTON (*Arch. Surgery*, 1928, v. 17, 324) reported one case from Virginia and eight others in the literature. CH'IN (*Chinese Med. J.*, 1933, v. 47, 1373) reported on a case of acute haemorrhagic pancreatitis due to *Ascaris* impacted in the ampulla of Vater, and gave 28 references to biliary and pancreatic ascariasis. CH'IN [this *Bulletin*, 1937, v. 34, 24] reported on a subject with ascariasis of the liver which caused fatal haemorrhage into the biliary tract and thence into the alimentary canal and peritoneal cavity. CHEN (*Chinese Med. J.*, 1943, v. 61A, 51) reported three cases of biliary ascariasis, one of which is the first now referred to by the present authors, who report on 19 cases seen in hospitals in Chengtu during the last 3 years.

All the present authors' subjects complained of severe epigastric pain, or pain in the right upper quadrant (one subject had pain in the epigastrium and left upper quadrant). The authors consider a "distending" pain more characteristic of biliary ascariasis than the stabbing kind of pain due to cholelithiasis. All but three of the patients vomited. The general symptoms suggested cholecystitis. Jaundice was present in five; all but two had eggs of *Ascaris* in the stools. The temperature was low. Ten of the patients had had similar attacks before. Three of them had cholecystitis, four had distended gall bladders and five had tense, firm common bile ducts, through the walls of which ascarids could be seen; six had dilated bile ducts. Ascarids were present in the common bile duct of all. Typically, the anterior one-third

of an ascarid, 20 cm. long, projected into one of the hepatic ducts, the remaining part of the nematode extending down the common bile duct to the duodenum. In three subjects there were ascarids either partly or completely in the gall bladder as well as in the common bile duct.

The authors comment on the " predilection " of *Ascaris* to enter any available opening. They have been found projecting through holes in swallowed glass beads or buttons, and in the appendix ; if no openings are available, they burrow into tissues. More serious consideration should be given to biliary ascariasis. If, in an area in which *Ascaris* is endemic, a young person below the usual age for cholelithiasis shows symptoms of disease of the biliary tract, biliary ascariasis should be suspected. This diagnosis is reasonable if the stools contain eggs of *Ascaris*, if there is a recent history of ascariasis, if ascarids have been vomited recently, if there is a history of similar previous attacks and if the subject has the characteristic peculiar " distending " pain. [See also GUHL, this *Bulletin*, 1945, v. 42, 51.] *G. Lapage.*

ASHBURN, L. L., PERRIN, T. L., BRADY, F. J. & LAWTON, A. H. **Histologic Changes in Ovary and Uterus of Live** *Dirofilaria immitis* **recovered from Dogs treated with Trivalent Antimony Compounds.** *Arch. Pathology.* 1945, Nov.–Dec., v. 40, No. 5, 334–9, 2 figs.

We have little knowledge of the effects upon nematodes of drugs used for the treatment of infestations with them. The authors treated dogs infested with *Dirofilaria immitis* with antimonial and mercurial compounds, and studied histologically the effects of these drugs upon the ovaries, and upon the developing ova and microfilarial larvae in the uteri of the nematodes.

ITAGAKI and MAKINO [this *Bulletin*, 1927, v. 24, 995] noted that there were no embryos in the uteri of " worms " recovered from the heart of one dog eight and a half months after it had been treated with sodium antimonyl tartrate. WRIGHT and UNDERWOOD (*Vet. Med.*, 1934, v. 29, 234) found no embryos in the uteri of adult " worms " removed from dogs killed after the 37th day of treatment with Fouadin. WRIGHT and HARWOOD [see CHRISTIE, this *Bulletin*, 1944, v. 41, 139] state that some observations indicate that the sterilization of female *Dirofilaria immitis* was due to fatty degeneration and necrosis of the reproductive cells of the ovary. [They also summarize our knowledge of the mode of action of anthelmintics.] BROWN and SHELDON [*ibid.*, 1942, v. 39, 190] could not find microfilarial larvae in the uteri of female nematodes recovered alive from dogs treated with a combination of Fouadin and sulphanilamide. LAWTON *et al.* [*ibid.*, 1946, v. 43, 55] report the elimination of circulating microfilarial larvae by 23 out of 24 trivalent antimonial compounds, and the failure of mercurial compounds in this respect.

The present authors examined specimens of *D. immitis* recovered from 25 dogs treated with various antimonial compounds, and from two dogs treated with mercurial compounds. [No list of these compounds is given.] Microfilarial counts were made from samples of the blood of the dogs each time the drugs were given (6 days a week). As controls 15 female *D. immitis* were used, 10 being obtained from five untreated dogs and 5 from two dogs which died 2½ hours after a single dose of one of the drugs being tested. The worms were wound round glass tubing and the ends fixed with rubber bands. They were then fixed in 1 : 10 solution of formaldehyde U.S.P. The nematodes were dehydrated in acetone, cleared in benzene and cedar oil, and embedded in 56°C. paraffin wax. The stains used were haematoxylin azure eosinate [see LILLIE, *Stain Technology*, 1941, v. 16, 1] and van Gieson's stain. All the descriptions given refer to the posterior ovaries ; anterior ovaries were never

seen. For the details of the appearances seen, the paper and its illustrations must be consulted.

It was evident that at least temporary sterilization of female *Dirofilaria* could be accomplished by treatment of their hosts with antimonial compounds. Eight sterilized *Dirofilaria* were obtained from eight dogs treated with these compounds, 70 to 107 days after completion of treatment. Longer observation is required to determine whether the sterilization of *Dirofilaria* is permanent. BROWN [this *Bulletin*, 1945, v. 42, 53] found that treatment of patients with lithium antimonyl tartrate reduced the microfilarial count 85 to 100 per cent. in 4½ to 5 months, and thought it likely that the filarial nematodes had been killed. The present authors, however, think it likely that the nematodes were sterilized, for they found females of *Dirofilaria immitis* which were sterilized 3½ months after the end of the treatment. Such a result would be valuable, because it would reduce the degree of infestation of the mosquito intermediate hosts. The authors think that, although direct action of the drugs on the microfilarial larvae and on multicellular ova may have caused the absence of these developmental stages, it is more likely that the drug acted directly on the earlier stages of development, so that the microfilarial stage was never reached. The presence of degenerate ova in the uteri of some *Dirofilaria* up to 107 days after treatment of the dogs had ceased, is not likely to have been due to persistence of the necrotic material for so long; some of these degenerate cells had retained their form, which suggests that their degeneration had been recent; the authors therefore suggest that, although the ova were shed into the uterus, they had been injured so much that they could not develop, or that the worms retained the drug so long that the ovaries were influenced by it for some time after treatment ended.

Thus the therapeutic compounds used caused changes in the ovary, the developing ova and microfilarial larvae, which agreed well, in most instances, with the microfilarial counts of the circulating blood. The changes seen were early degeneration or necrosis of the ova and the absence of microfilarial larvae from most of the females. The uteri of some females were entirely empty, and there were areas of necrosis in their ovaries. The worms taken from two dogs treated with mercurial compounds were normal. *G. Lapage.*

WILLIAMS, R. W. & BROWN, H. W. **The Transmission of** *Litomosoides carinii*, **Filariid Parasite of the Cotton Rat, by the Tropical Rat Mite,** *Liponyssus bacoti*. *Science*. 1946, Feb. 22, 224.

Cotton rats, *Sigmodon hispidus*, infected with the filarial worm *Litomosoides carinii*, were kept separately in cages in boxes, and tropical rat mites, *Liponyssus bacoti*, were added to infest the rats and multiply on them. Two white rats in separate cages were afterwards placed in the boxes alongside the cages of the cotton rats and became infected with the filaria. Control white rats similarly placed near infected cotton rats but in the absence of the mites, did not become infected with the filaria. It was concluded that the tropical rat mite serves as a vector of this worm.

Adult *L. carinii* were found in the pleural cavity of the white rats after 42 and 44 days, respectively; in one rat the worms were from 1·165 mm. to 12 mm. long, in the other rat they were 9 mm. and 42 mm. The control rats were negative when examined at 44 days.

In the infective stage in the mites the worms are from 800$\mu$ to 1,000$\mu$ in length and it is interesting that a worm only 165$\mu$ longer than the biggest worm in a mite was found in the pleural cavity of one of the white rats; this suggests either that the worm reaches the pleural cavity very quickly or that it grows very slowly before reaching the pleural cavity.

Microfilariae were seen in the blood of both cotton and white rats, experimentally infected by mites, after 80 days and it is thought that they may appear as early as 50 or 60 days after exposure to infection. *J. F. Corson.*

GOLDMAN, L. & ORTIZ, L. F. **Types of Dermatitis in American Onchocerciasis.** *Arch. Dermat. & Syph.* 1946, Feb., v. 53, No. 2, 79–93, 7 figs.

A description of some of the forms of dermatitis found in association with onchocerciasis in Chiapas, Mexico, a district where the endemicity of the disease is high. There are difficulties in deciding what forms are due actually to *Onchocerca* infestation and what to associated conditions, such as pruritus from mycotic infections, pinta, tropical ulcers, syphilis, etc.

The authors first give a list of " cutaneous reactions " observed in patients with onchocerciasis and this includes " scarring from cutaneous biopsies or excision of nodules " and " dermatitis from therapeutic agents " neither of which could strictly be called dermatitis in onchocerciasis, nor could " reactions to the bite of simuliid " which might or might not be carrying *Onchocerca*. They then describe in detail three forms of dermatitis definitely associated with onchocerciasis, namely, the pigmentation dermatitis, or *mal de morado* (purple disease), a lichenoid form, and an eczematoid dermatitis.

In the first of these the skin may be dry or wrinkled, but is usually smooth, of a bluish-red or purple (morado) colour, perhaps with local oedema ; biopsy reveals microfilariae in the upper part of the dermis. Most of those with this condition have previously had onchocerca nodules. It may be associated with pruritus and oedema. The face is often involved and puffiness with oedema and eosinophilia are reminiscent of trichiniasis.

The second or lichen type chiefly affects the face and may occur with the third type (see below), but may also affect the arms and, less often, the legs. The skin is thickened and hyperpigmented, and there is intense itching. Biopsy reveals microfilariae in the pars papillaris. In the third, the eczematoid type, there are papulo-vesicular, excoriated lesions, sometimes impetiginous, or there may be papillomatous, verrucose and hyperkeratotic patches on arms, hands and neck.

Treatment of these conditions comprises removal of onchocerca swellings (onchocercomas) and local treatment of the cutaneous condition on the usual lines. *H. Harold Scott.*

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## DEFICIENCY DISEASES.

MUSSELMAN, M. M. **Nutritional Diseases in Cabanatuan.** *War Medicine.* Chicago. 1945, Nov.–Dec., v. 8, No. 5, 325–32.

This is a straightforward account of the experiences of a U.S. army doctor imprisoned by the Japanese in the Philippines. Rations were short during the period of resistance on the Bataan peninsula, and after surrender in April 1942, the ration allowed consisted of about 300 gm. rice, 30 gm. flour, 10 gm. sugar, 10 gm. oil and 100 gm. leaves and stems of vegetables or vines, with occasionally about 5 gm. of carabao meat. This diet provided less than 1,500 calories, less than 30 gm. protein, and very small amounts of vitamins.

Swollen ankles were noted early in many of the men, while some had generalized oedema : soon 25–50 per cent. had symptoms of beriberi with neuritis and oedema. Signs of pellagra took longer (4–8 months) to appear but then progressed rapidly. A home-grown culture of yeast was prepared in sufficient quantity to ameliorate the symptoms of the worst sufferers, but was insufficient to produce cure.

By late October 1942, 90 per cent. of the prisoners suffered from malnutrition, and fully 50 per cent. were seriously ill with beriberi, pellagra, malaria, dysentery or other infectious diseases. The fever, anorexia, digestive disturbances and diarrhoea associated with these latter diseases contributed to the deficiency states. Symptoms of optic neuritis appeared in over half the prisoners, while cerebral, spinal and peripheral nerve lesions gave many variations to the clinical picture.

The arrival of Red Cross supplies was followed by an improvement in the diet, and in most cases by a rapid improvement in the physical condition of the prisoners. The ending of these extra supplies was marked by a return to the previous deficiency states, again alleviated by a fresh supply while this lasted.

In the summer of 1944, men doing hard labour were issued with food supplying less than 1,000 calories a day, while the remainder received less than 800 calories. After this extreme reduction, many men were seen to have attacks of hypoglycaemia.

In the autumn of 1944, after a widespread epidemic of dengue, about a third of the 500 men in one camp showed a symptom complex similar to myasthenia gravis. Its aetiology and nature were never clearly defined, and the condition tended to disappear.

After release of the prisoners from captivity, and their return to a full diet, the gain in weight, the clearing of pellagrous lesions, the loss of oedema and the improvement in the neurological lesions were remarkable. It is felt, however, that complete recovery is unlikely in patients with advanced nerve lesions.

Scurvy never constituted a serious problem. A long delay in the healing of wounds was an embarrassing surgical problem that may have been determined in part by subclinical scurvy. *H. E. Harding.*

MUSSELMAN, M. M. **Pellagra in Americans in a Japanese Prison.** *Bull. U.S. Army Med. Dept.* 1946, Apr., v. 5, No. 4, 403–11.

After 6–7 months on a diet affording less than 1,500 calories, less than 30 gm. of protein most of which was of vegetable origin, and very small amounts of vitamins, pellagra was observed in rapidly increasing numbers of prisoners. Within a short time almost every prisoner showed some signs of the condition, while half of them had fairly severe lesions of the mouth and skin. Administration of a thin culture of air-borne yeasts was of marked therapeutic value, but the quantities available allowed treatment of only the more severe cases.

After the receipt of Red Cross supplies the general condition improved markedly, only to relapse with the exhaustion of these supplements. It was noted that pure preparations of vitamins were more effective when the diet was more adequate.

[See also paper by MUSSELMAN above.] *H. E. Harding.*

SOUTH AFRICAN RED CROSS SOCIETY (NATAL BRANCH). **Report to the Red Cross Society, Natal, on an Experiment with Pre-Digested Protein** [DORMER, B. A.]. 20 pp., 8 charts & 15 pls.

Dr. Dormer reports that the death rate from tuberculosis has risen from 250 to 700 per 100,000 in some industrial areas of South Africa during the war, and he also finds a great increase in severe oedema in native children, and in frank nutritional deficiency diseases in adults. Much of this increase he believes is connected with a lowered standard of nutrition and in particular with a lessened intake of protein.

Colonel Watkins Pitchford has worked out a method of enzymic digestion of whale flesh that produces stable concentrations of amino acids or mixtures

of these acids with polypeptides, peptones, etc. Whale flesh is commonly almost completely wasted, and large amounts of it could be made available in this manner. The products are bitter and unpalatable, but their taste can be disguised in soups, wines, chocolates, toffees and biscuits.

Experimental trials of these products have given very favourable impressions to their users. Patients with pulmonary tuberculosis, who were previously losing weight steadily, have in most cases gained weight, and their general condition has improved. Similar results have been obtained in a few patients with tuberculous enteritis. It is not claimed that feeding with these mixtures is a cure for tuberculosis, but the improvement produced in the patient's condition sometimes allows active therapy to be undertaken.

Native children suffering from malignant oedema or infantile pellagra have shown rapid improvement when treatment is started with these products and glucose. Tropical ulcers have been found to heal rapidly. Feeding with these protein digests is also recommended for patients with peptic ulcers, nephrosis, hepatitis, diabetes, hyperthyroidism, anorexia nervosa, and various allergic states.

[This is a report to the South African Red Cross Society urging an extension of the support given to Colonel Watkins Pitchford. It is not meant to be a properly documented scientific report. Judged, however, on the very lowest level it does draw attention to the very serious effects of malnutrition in South Africa, and it points to a hitherto untapped source of protein.]

*H. E. Harding.*

GILLMAN, J., MANDELSTAM, J. & GILLMAN, T. **A Comparison of Chemical and Histological Estimations of the Iron and Copper Content of the Livers of Africans in relation to the Pathogenesis of Cytosiderosis and Cirrhosis (Haemochromatosis).** *South African J. Med. Sci.* 1945, Dec., v. 10, No. 4, 109–36, 7 figs. on 1 pl. [60 refs.]

A comparison of the amount of iron assessed by histological methods and that found by chemical analysis in 73 livers showed fairly good correlation. It was found that iron might be visible histologically without any increase in the quantity found chemically, *i.e.* that normally bound and invisible iron could become visible. Livers from pellagrins were classified in four types [GILLMAN and GILLMAN, this *Bulletin*, 1946, v. 43, 364]. On the whole this typing was found to correspond with increasing quantities of iron determined chemically, but there was considerable overlap between individual livers in each group.

Cirrhosis and pigmentation are separate conditions. Extensive cirrhosis may exist without a significant increase in the amount of iron: iron may be present in quantities as great as those described in haemochromatosis, without any cirrhosis: cirrhosis may be found with very varying quantities of iron, which may be in liver cells only, or in the portal tracts as well.

The amount of copper in the liver does not vary directly with the amount of iron, but with a marked increase in the latter there is usually an increase in the former.

[Although frequently quoted in the text, Sheldon's book—Haemochromatosis, Oxford 1935, does not appear in the list of references.]

*H. E. Harding.*

WINTROBE, M. M. **Relation of Nutritional Deficiency to Cardiac Dysfunction.** *Arch. Intern. Med.* 1945, Nov.–Dec., v. 76, No. 5, 341–6. [Refs. in footnotes.]

A brief review of the literature on cardiac beriberi is followed by a summary of the work at the University of Utah on the cardiac changes in pigs given a

diet deficient in thiamin. In these animals thiamin deficiency leads to severe changes in cardiac function, and produces well defined histological lesions. It is still undecided whether a deficiency of thiamin produces similar changes in man. The lesions found in pigs are unlike those that have been described as occurring in the heart in beriberi, and resemble more those that have been described under the title of " isolated myocarditis " or " Fiedler's myocarditis".

*H. E. Harding.*

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## SPRUE.

BLACK, D. A. K., FOURMAN, L. P. R. & TRINDER, P. **Fat-Absorption in Tropical Sprue.** *Lancet.* 1946, Apr. 20, 574–5.

[A piece of work of no little importance to those interested in the study of the problems of sprue.] The authors have carried out experiments to determine the degree of fat-absorption in sprue at an early stage. All the patients suffered from steatorrhoea and had lost weight, some had glossitis and showed signs of macrocytic anaemia. The percentage of fat-absorption was determined by the formula

$$\frac{(\text{Dietary fat—excreted fat}) \times 100}{\text{Dietary fat}}$$

In untreated patients with sprue in various stages, but with formed stools, the absorption ranged between 51 and 85 per cent., with an average of 75·6 per cent. ; three others, with watery diarrhoea, had, generally, a lower absorption, 30, 55 and 64 per cent. In the cases of five patients the fat content of the diet was raised by about 40 per cent., from 69 to 96 gm. a day. As a result more fat was excreted but there was little change in the proportion absorbed ; in two it remained practically the same (82 and 85 in place of 83 and 87 per cent.), in one it rose slightly (83 to 88), in two it fell (from 80 and 51 to 74 and 44 respectively). The natural inference is that moderate increase in dietary fat has little effect on absorption.

Giving nicotinic acid, riboflavin or pantothenic acid did not improve the absorption. The effect of liver is more remarkable ; though the stomatitis and glossitis improved and weight was gained, fat-absorption was not affected unless there was diarrhoea ; in such patients improvement of the diarrhoea was accompanied by increased fat-absorption. Giving of a yeast extract of the Marmite type seemed to increase fat-absorption ; this may be due to its folic acid content. The question is to be the subject of further study.

From the investigations so far carried out the following points emerge : (1) Intestinal secretion of fat does not play an important part in causing steatorrhoea, for the latter disappears on a very low fat diet. (2) Sprue is not due to diminished motility of the villi or reduced absorptive surface, because the absorption percentage remains almost constant when the intake of fat is moderately increased. (3) This constancy " is more easily explained by theories based on the failure of an enzyme system such as that concerned in phosphorylation." [See STANNUS, this *Bulletin*, 1943, v. 40, 259.]

*H. Harold Scott.*

DARBY, W. J., JONES, E. & JOHNSON, H. C. **The Use of Synthetic *L. casei* Factor in the Treatment of Sprue.** *Science.* 1946, Jan. 25, 108.

DAY *et al.* (*J. Biol. Chem.*, 1945, v. 157, 423) showed that vitamin M deficiency in the monkey is promptly cured by the injection of purified *Lactobacillus casei* factor, and this led the authors of this paper to try synthetic *L. casei* factor (Lederle) (1)[3] in the treatment of three cases of sprue.

Crystalline synthetic *L. casei* factor was dissolved in water with a small quantity of disodium phosphate, and the solution was autoclaved ; 15 mgm. of the factor in this solution were injected intramuscularly daily. Improvement, both clinical and haematological, followed rapidly in all three patients ; the symptoms of glossitis disappeared within 3 or 4 days and the lingual papillae were regenerated ; the diarrhoea ceased, the appetite improved, and the body weight increased, one patient gaining 26 lb. in the first 6 weeks. There was a great increase in the numbers of reticulocytes, blood platelets and blood leucocytes, and some increase also of haemoglobin and of erythrocytes ; sternal puncture showed improvement in the bone marrow.

This striking response to the treatment suggested to the authors certain possible relationships : the synthetic *L. casei* factor is probably identical with, or closely related to, the substance in liver extract which is effective in the treatment of sprue, this syndrome and that of vitamin M deficiency in the monkey being similar (LANGSTON *et al.*, *J. Exper. Med.*, 1938, v. 68, 923) ; since the factor which relieves the macrocytic anaemia of pregnancy is closely allied to vitamin M, the synthetic *L. casei* factor may be efficacious in the treatment of that form of anaemia ; the *L. casei* factor may be related to the erythrocyte maturating factor, since in sprue and pernicious anaemia the blood picture, the bone marrow, and the glossitis are similar.

SPIES *et al.* (this *Bulletin*, 1946, v. 43, 375) found that synthetic *L. casei* factor was effective in the treatment of incompletely diagnosed macrocytic anaemia and GOLDSMITH (personal communication) reported the successful treatment of " nutritional macrocytic anaemia " with " folic acid".

The authors' references include also : DAY (in " Vitamins and Hormones " ed. by HARRIS and THIMANN, 1944, New York, *Acad. Press Inc.*, v. 2, 71) ; WILLS and STEWART [*Bulletin of Hygiene*, 1936, v. 11, 136]. [Other references to macrocytic anaemia are : this *Bulletin*, 1938, v. 35, 846 ; 1939, v. 36, 422 ; 1940, v. 37, 883–5 ; 1941, v. 38, 184 ; 1942, v. 39, 482, 483 ; 1943, v. 40, 405, 484, 938 ; 1945, v. 42, 59, 222, 308, 482 ; 1946, v. 43, 146.]

*J. F. Corson.*

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## HAEMATOLOGY.

DA SILVA, E. M. Estudos sôbre indice de siclemia. [**Studies on the Sicklaemia Index.**] *Mem. Inst. Oswaldo Cruz.* 1945, Apr., v. 42, No. 2, 315–40, 10 figs. [47 refs.] English summary.

The sickle cell trait may be detected by several well-known methods. For a rapid determination, the blood may be exposed to a current of carbon dioxide. For large scale surveys, coverglass preparations of either fresh blood or blood mixed with an isotonic anticoagulant solution are useful. The addition of anti-A or anti-B agglutinating serum does not check sickling, so that by such combinations the blood group and the sickle cell trait may be determined at the same time. Similarly the addition of solutions of brilliant cresyl blue may be used for the simultaneous determination of the degree of reticulocytosis and the sicklaemia. For the study of the process of sickling, mixtures of blood and isotonic anticoagulant may be sealed in tubes and sampled at intervals, the cells being fixed by the addition of formalin at the time of sampling. Finally, maceration in isotonic saline or fixative solutions, of tissues preserved in alcohol or formalin, may enable a retrospective determination of sicklaemia to be made after a period as long even as 26 years.

Among a heterogeneous group of 1,130 negroes and negro cross-breeds, 113 sicklaemic individuals were found, giving an index of approximately 10 per

cent., whereas among 30 Mongoloid and 120 Caucasoid individuals no example of sicklaemia was found.

In 58 sicklaemic persons with morbid conditions producing circulatory stasis, anatomico-pathological changes of sickle cell anaemia were not observed. These findings contradict the hypothesis that stasis is a sufficient factor for the transition from a sicklaemic to an anaemic condition. In 13 sicklaemic persons infected with malaria no symptoms of sickle cell anaemia were observed, but it was also verified that parasitism by *P. vivax* does not check sickling.

It is important, when determining sicklaemic indices, to take into consideration the direct hereditary factor, as the index for a familial group may be much larger than that obtained by random sampling; to differentiate the familial incidence the term "familial sicklaemia index" is suggested. Sickle cell anaemia may only be obvious at times in generations very distant one from another, giving rise to a "skipping phenomenon"; in such cases the condition is maintained in the intervals through sicklaemic individuals who may be regarded as potentially diseased, or as healthy carriers of a pathogenic feature.

The systematic and periodical examination of sicklaemic individuals is urged, as such investigations may throw light on the genetically transmitted factors, and also on the intrinsic and extrinsic factors associated with the disease. Control of the condition would also be aided by a census of sicklaemic individuals, and remarks on their identification cards, by the systematic examination for sicklaemia of all the newly-born, by the supervision of all sicklaemic individuals, who should be required to present themselves to the public health authorities periodically and especially on the appearance of any symptoms of the disease, and finally by the inclusion of tests for sicklaemia in prenuptial medical examinations. *F. Murgatroyd.*

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## VENOMS AND ANTIVENENES.

MARTIN, W. B. **Clinical Experience with Snake Bites on Okinawa.** *Bull. U.S. Army Med. Dept.* 1946, Jan., v. 5, No. 1, 79–82.

Nine cases of snake bite which occurred during the Okinawa campaign are described. Four case reports are given in full. In all instances in which the snake was identified, it was the Habu (*Trimeresurus flavoviridis*). There were no fatalities. Clinically, there was a rapid onset of symptoms with brief, local anaesthesia in some cases, followed by pain and swelling and systemic disturbance. The venom was mainly haemotoxic and had no effect on the brain centres.

Treatment recommended includes "criss-cross incisions" over the site of the fang marks, suction immediately and "intermittently for 12 hours"; and, if the bite is in a limb, the application of a tourniquet "tight enough to prevent venous return but not enough to compress the arteries, and it should be released every 20 minutes and replaced at higher levels if the swelling is progressing proximally." The authors advise the administration of Nearctic antivenene, although none of their cases was treated in this way. Penicillin should be given in doses of 20,000 units 3-hourly (after an initial dose of 30,000 units), in view of the penetrating wound and local oedema.

[No mention is made of washing the site before the incision in order to remove ejected venom.] *B. G. Maegraith.*

ARANTES, J. B., KARMANN, G. & BIER, O. G. Emprêgo da reação de floculação específica na dosagem do antiveneno crotálico. [**Applicability of the Specific Flocculation Reaction for the in vitro Titration of Crotalic Antivenene.**] *Mem. Inst. Butantan.* 1944–1945, v. 18, 21–6. English summary (7 lines).

BIER, O. G. Estudo quantitativo da reação de floculação entre o veneno e o antiveneno crotálico. [**A Quantitative Study of the Flocculation Reaction between the Venom of** *Crotalus t. terrificus* **and its Specific Antivenene.**] *Mem. Inst. Butantan.* 1944–1945, v. 18, 27–32. English summary (8 lines).

GRASSET, E., SCHAAFSMA, A. & HODGSON, J. A. **Studies on the Venom of South African Scorpions** (*Parabuthus, Hadogenes, Opisthophthalmus*) **and the Preparation of a Specific Anti-Scorpion Serum.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 397–421, 3 figs. on 2 pls. [19 refs.]

In South Africa, cases of scorpion sting are not infrequent, but, as elsewhere where scorpions abound, fatalities are rare and occur mostly in children. Much work has been done on the taxonomy and systematics of South African scorpions, but little on their relative toxicity. The authors in this paper record their investigations on three genera: *Parabuthus*, especially *P. transvaalicus* and *P. triradulatus* from the northern Transvaal and Bechuanaland; this genus is common throughout Africa and Arabia but is not found in Natal and Pondoland. *Hadogenes*, especially *H. troglodytes dentatus*, found in South Africa, Portuguese East Africa, the Congo and Madagascar, but not along the coast from Capetown to Port Elizabeth. *Opisthophthalmus*, especially *O. walberghi* and *O. glabrifrons* from Bechuanaland.

For experiment, venom was obtained from *Parabuthus* by aspiration with a pipette after the tip of the telson had been cut; from the others, which had more delicate telsons, by squeezing out with forceps. In each case, the venom, a white milky fluid, was collected on a watch-glass and allowed to dry. The average yields of dried venom for each scorpion were *Parabuthus* 4·8 mgm., *Hadogenes* 2·7 mgm., *Opisthophthalmus* 1·4 mgm.

For their experiments the authors prepared saline solutions standardized to contain 10 mgm. per cc., and the animals used were mice, guineapigs, rabbits and pigeons, injections were made intravenously, subcutaneously, intramuscularly, intracutaneously and intracerebrally. In solution the venoms are unstable, so all experiments were made with freshly prepared solutions. The results were as follows:—

*Parabuthus* venom. White mice, average weight 22 gm.; 0·1–0·4 mgm. intravenously caused immediate dyspnoea, staggering and inco-ordination, extension of hind legs, or gasping, uncontrolled jumping and paralysis; death occurred in ½ to 5 minutes with progressive paralysis and asphyxia. Subcutaneously, the symptoms were similar but the dose needed was four times the intravenous dose. 0·002–0·1 mgm. intracerebrally produced immediate convulsions, trembling, paralysis and death, in a few seconds with the larger dose. In other animals the symptoms were similar; the dosage for guineapigs of 350–400 gm., was 1–2 mgm., subcutaneously or intramuscularly; for rabbits of 2,000 gm., 5 mgm. intravenously; in pigeons of 400–450 gm., with 0·8–1·5 mgm. intravenously there were marked neuromotor symptoms. To epitomize: *Parabuthus* venom is neurotoxic, producing at first neuromuscular excitability and dyspnoea from action on the respiratory centre, followed by paralysis and asphyxia.

*Hadogenes* venom. 0·4–0·6 mgm. intravenously in mice caused dyspnoea and paralysis, and death within 15 minutes. Subcutaneously, large doses, up to 40 mgm., produced hyperexcitability for 1–2 hours, then trembling and

increasing prostration and death in 3 to 40 hours. With guineapigs, large doses, to 185 gm. subcutaneously, were needed to produce these symptoms, and a local saccular oedema occurred ; 80 mgm. intramuscularly caused redness and swelling, but was not fatal. In rabbits, 50 mgm. intravenously caused death in 15 minutes. In pigeons, 6–8 mgm. intravenously killed in 10 minutes or less, but as much as 125 mgm. were needed intramuscularly or subcutaneously to kill, in 10 minutes by the former route, in 4–12 hours by the latter.

*Opisthophthalmus* venom. 2–3 mgm. were needed intravenously to kill mice in 1–20 minutes, the symptoms of excitability, dyspnoea and paralysis resembling those with the other venoms. Subcutaneous and intramuscular injections in doses of 20–80 mgm. in guineapigs differed from the other venoms in producing severe local haemorrhagic swelling, gelatinous oedema and later sloughing ; the same occurred in pigeons. These routes were not tried with rabbits.

As regards haemolysis, this effect occurred with all the venoms, but only in relatively high concentrations, such as 20 mgm. per cc. ; guineapig erythrocytes were haemolysed more readily than sheep's cells and the haemolysis was less marked with *Parabuthus* venom than with either of the others.

The effects of heat were observed, at 70°C. in a water-bath for ½ hour ; at boiling point for 30 minutes, and for 90 minutes ; the toxicity of the venoms remained practically unchanged. In high concentration of 10–30 mgm. per cc., the *Parabuthus* venom had a graded proteolytic action on gelatin *in vitro*, the other two had no such action.

Tests with antivenenes of *Naja flava* and *Bitis arietans* showed them to be ineffectual against these scorpion venoms. Preparation of specific antiscorpion serum from horses was undertaken, starting with toxoid and continuing with natural venom. Practitioners were asked to report on the results of the use of these antivenenes, and so far, though only a few reports have come in, they appear to be favourable when the serum is injected intramuscularly in a dose of 10 cc. *H. Harold Scott.*

TINKHAM, E. R. **A Poison-Squirting Spider.** *Bull. U.S. Army Med. Dept.* 1946, Mar., v. 5, No. 3, 361–2.

A soldier in Florida, U.S.A., while inspecting the tail lamp of his motor cycle one day at noon, saw a spider about 12 to 15 in. distant and disturbed it ; at that moment he felt something enter his eye and it caused him great pain. His eye became inflamed, conjunctivitis persisting for two days. He thought the spider had squirted something from its mouth into his eye, while another soldier who was present thought it had squirted from its abdomen. The spider was caught and was identified as *Peucetia viridans*, the identification being confirmed afterwards, from the author's drawings and description, by H. J. GERTSCH, arachnologist, American Museum of Natural History, New York, who, however, stated that this species was not known to squirt venom and that he knew of no other spider with that reputation except, perhaps *Scytodes* which captures its prey by spitting on it from a short distance.

*J. F. Corson.*

## DERMATOLOGY AND FUNGUS DISEASES.

VARELA, G. Estudios serológicos y cardiovasculares de un grupo seleccionado de enfermos de "mal del pinto." [**Serological and Cardiovascular Studies on Pinta Patients.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Sept., v. 6, No. 3, 163–6.

Twenty-nine patients suffering from mal del pinto, whose ages ranged between 4 and 20 years, were selected because they had not received any treatment for their disease and gave no history of having been infected with syphilis. Tests were made with their sera and cerebrospinal fluids for complement fixation, and the reactions of Pandy, Nonne-Apelt and Mazzini were carried out with the cerebrospinal fluids. Radiograms were taken of the heart and electrocardiograms made.

Some previous investigators have recorded positive results with the c.s.f.; for example, the Mexican Commission on Pinta in 1930 (number of cases not stated) reported Wassermann reactions markedly positive; PARDO CASTELLO in 1936 recorded 4 out of 26 as having an increase in globulin and one with a positive Wassermann reaction and positive Kahn. GRAU and TRIANA in 1937 recorded two positive out of 12. On the other hand, BOTERO in 1939 and LEÓN BLANCO in 1942 found no change in the fluid of 69 and 53 patients, respectively. The present author's investigations support the last-named. The sera in all his patients gave a marked positive reaction but the cerebrospinal fluids were, without exception, negative. The electrocardiograms also showed no departure from the normal, though three showed by X-rays an increased area of the aorta. *H. Harold Scott.*

DOBES, W. L. & JONES, J. **Erythema Streptogenes.** *Arch. Dermat. & Syph.* 1946, Feb., v. 53, No. 2, 107–14, 4 figs. [12 refs.]

Dermatoses associated with streptococci are common, but the condition described in this paper does not appear to have found a place in the textbooks. It is a dry dermatitis, seen in Europeans as well as natives, but more often in the latter and in children, in the authors' experience. The eruption may appear anywhere, but is most common on the face. There is first an erythema which fades in a week or two, when a scaliness is seen and depigmentation sets in, and in 2–3 months there is a depigmented patch, with ill-defined border (thus differing from the more marked and sharply defined areas of vitiligo); the affected areas are smooth or show a fine branny desquamation. Scrapings from the lesions were taken from seven patients. In two cases there was no growth, though repeated attempts were made; the condition had existed for 8 months in one and 12 months in the other, and may have been receding. In the other five, haemolytic streptococci were isolated (in one case together with a haemolytic *Staphylococcus aureus*); the duration of these positive cases ranged between 3 and 18 months. The best treatment is local rubbing in of a crude tar ointment; pigmentation usually returns in about 3 months. That the condition is actually caused by the streptococcus is not proved, but it is maintained that "streptococci on the normal skin of persons in good health can never be considered as saprophytic." *H. Harold Scott.*

BADHWAR, R. L., NAYAR, S. L. & CHOPRA, I. C. **Indian Plants liable to produce Dermatitis.** *Indian J. Agric. Sci.* 1945, June, v. 15, Pt. 3, 155–71. [46 refs.]

In India some 76 plants are known to produce irritation of the skin and even actual dermatitis in certain persons; all are not equally susceptible. The

mode of action differs. Plants causing direct mechanical injury, as by penetration of spines and thorns, wounds from which may subsequently become infected and so set up dermatitis, are excluded from this article. Included are :—

(1) Those of the *Rhus* type and allied genera whose sap exudes when the plant is injured ; contact with the sap sets up a dermatitis due to a phenolic oily resin which it contains, and which is known as toxicodendrol. It is not itself volatile, but it may be conveyed in the soot of burning plants and also by insects which have alighted on an injured plant. Claim has been made that it is present in the pollen, but, say the authors, this is not so. The irritation may be relieved by alkaline applications, and a brief immunity can be produced by subcutaneous injection of an alcoholic extract, but this immunity is very transient, not lasting for more than a month.

(2) A second type of irritant is the *Urtica* type ; nettles are examples and the most potent of these in India is *Laportea crenulata*, the Fever nettle or Devil nettle. When the fragile hairs of the nettle penetrate the skin they break, and the irritant in the hair enters the tissue. The protoplasm of the hairs is alkaline but encloses an acid cell-sap which contains formic, acetic, butyric and other volatile fatty acids.

(3) A third group comprises plants which, when ingested, produce photosensitization and consequent dermatitis of unpigmented parts. Examples of this group are *Fagopyrum esculentum* and *Hypericum perforatum*.

Lastly, there is (4) a miscellaneous group, *e.g. Xanthium strumarium*, which produces dermatitis in a few who happen to be sensitive to it ; the toxic principles are still undetermined. In others, *e.g. Erigeron canadensis*, there is an irritating essential oil ; in *Podophyllum hexandrum* it is a resin in the rootstock which is the irritant ; in other cases the mechanism is not known ; dust from dried plants may irritate the nasal and ocular mucosa.

The authors present in a table a list of the 76 plants known in India to cause dermatitis ; they give also the English and vernacular names, their geographical distribution, the part of the plant responsible for causing the dermatitis and, where known, the toxic principle in each case. [A valuable piece of work.]

*H. Harold Scott.*

MENDELSOHN, H. V. **Lemon Grass Oil : a Primary Irritant and Sensitizing Agent.** *Arch. Dermat. & Syph.* 1946, Feb., v. 53, No. 2, 94–8.

On the publication of his report of eight cases of dermatitis venenata due to lemon grass oil [see this *Bulletin*, 1945, v. 42, 66] the author received samples of the oil from three sources ; one from Florida containing 75 per cent. of citral, an aldehyde constituent of the oil ; another from India also containing 75 per cent., and a third from Guatemala with 76·2 per cent. He also received three samples of ionones, in which the aldehyde is converted into a ketone. They are highly aromatic and are used in making perfumes and cosmetics.

The author made patch tests with all of these on 15 persons. All reacted with vesicles and bullae to the undiluted oils, indicating a direct irritant action ; dilution of the oil, 1 in 10 or more, might result in a delayed reaction after 6 days, indicative of induced sensitivity, *i.e.* the diluted forms acted as sensitizers and when the patients were tested again 3 weeks later with the diluted oils, erythema and vesiculation were observed on removal of the test patches after 48 hours' application. In no instance was there any reaction to the ionones.

*H. Harold Scott.*

NUÑEZ ANDRADE, R. Dermatitis causada por *Haematosiphon inodora* (Duges, 1892). [**Dermatitis due to** *H. inodora.*] *Medicina.* Mexico. 1946, Feb. 10, v. 26, No. 501, 45–51, 4 figs. English summary.

"1. The author reports 21 cases, in residents in Mexico City, of a type of Dermatitis caused by bites of the chicken-bug called Haematosiphon inodora (Duges, 1892).

"2. One of the cases had been diagnosed as urticaria by food allergy; another as Prurigo mitis, and the rest of them were considered as bites from bedbugs (Cimex lectularius).

"3. The dermatitis caused by the Haematosiphon inodora, was generally observed in all the inhabitants of the infected houses and furthermore almost all the houses in the same quarter were infested by the insects.

"4. This dermatitis is polymorphous, having the appearance of hives [a popular name for urticaria and other skin diseases], papules, vesicules, vesicopustules, scratches or scars.

"5. This dermatitis causes intense itching, burning sensations, pain and sometimes general malaise and a rise of temperature derived from secondary infections."

PFANNER, E. F. **Coccidioidomycosis at U.S.M.C. Air Station, Mohave, California.** *U.S. Nav. Med. Bull.* 1946, Feb., v. 46, No. 2, 229–36.

In view of the discovery of isolated cases of coccidioidomycosis at a Naval Air Station at Mohave, California, an investigation was made into the possibility of the station being situated in an endemic area of the disease. All the staff were subjected to the coccidioidin skin test as soon as possible after arrival at the station, and those on whom the result of the test was negative were tested again after an interval of about 4½ months. If the second test had a positive result it was assumed that infection had occurred in the interval between the tests. Twenty-three men who were found negative by the first test gave positive reactions at the second test and none of these had been exposed to infection outside the station in the interval. In addition to these 23, seven men who were coccidioidin negative on arrival at the station were admitted to hospital at some later time for an illness which was diagnosed as coccidioidomycosis, and all seven became sensitive to coccidioidin during their illness. Clinical descriptions are given of these seven cases.

As none of the 30 men referred to had visited any known endemic focus of coccidioidomycosis outside the station it was concluded that the infections must have occurred at the Mohave Air Station and that the vicinity of the station is an endemic area of coccidioidomycosis. *J. T. Duncan.*

TWINING, H. E., DIXON, H. M. & WEIDMAN, F. D. **Penicillin in Treatment of Madura Foot: Report of Two Cases.** *U.S. Nav. Med. Bull.* 1946, Mar., v. 46, No. 3, 417–29, 8 figs. [10 refs.]

The authors describe two cases of mycetoma; one caused by *Monosporium apiospermum* and the other by a newly-named fungus *Cephalosporium granulomatis* n.sp. Weidman and Kligman. In the first case the disease was of 7 years' duration and some of the bones of the tarsus and metatarsus were involved. Penicillin treatment was instituted and this resulted in considerable improvement in the condition of the foot, although new lesions continued to appear. After a total dosage of 3,700,000 units, the patient was discharged with a prognosis of possible cure. Relapse occurred, however, and, after a further course of 2,100,000 units of penicillin had been given ineffectually, the diseased foot

was amputated. In the second case the disease was of only two years' duration and was limited to the soft tissues of the foot. Penicillin was given in doses of 20,000 units every three hours until a total of 2,300,000 units had been given. Improvement was rapid and apparently permanent, and the patient was discharged from hospital six weeks after the conclusion of the penicillin treatment. *J. T. Duncan.*

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## HEAT STROKE AND ALLIED CONDITIONS.

SHELLEY, W. B. & HORVATH, S. M. **The Oral and Rectal Temperatures in Hot Environments.** *Bull. U.S. Army Med. Dept.* 1946, Apr., v. 5, No. 4, 459–61, 1 fig.

"A comparison of rectal and oral temperatures of men working in a very hot room (120°F., 36 per cent R.H.) environment showed the rectal temperature to range from 1·4°F. below to 3·9°F. above oral temperature, averaging 1·2°F. higher than the oral."

LADELL, W. S. S. **Changes in the Chloride Concentration of Sweat with Acclimatization.** *Biochem. J.* 1945, v. 39, No. 5, xlvii-xlviii.

"The chloride concentration in serial sweat samples from the arms of subjects working in a hot humid environment rises as the exposure continues." Sweat is always hypotonic, and the glands, therefore, must do work when they excrete sweat; less work is done if the sweat is more concentrated, and the phenomenon reported may therefore be a manifestation of fatigue. "Total salt loss is practically constant in a given individual from day to day for a given total of sweat lost so long as the rate of sweating remains the same." In rapid acclimatization there is no fall in sweat chloride concentration.

One subject lived in a hot room day and night, and after the first few days the chloride concentration of his sweat no longer rose with time; this was not due to salt lack. After the subject had left the hot room he lost this acclimatization effect. Other subjects, who were exposed to heat for some hours every day over a period of many months, showed the same effect, but less markedly; salt loss for heavy sweating became less, showing diminished liability of the sweat glands to fatigue. This diminution in salt loss from sweat, which occurs in hyper-acclimatization, should not be confused with the fall in chloride concentration in sweat which occurs as a result of deficiency of salt intake. *Charles Wilcocks.*

BURCH, G. E. & WINSOR, T. **Diffusion of Water through Dead Plantar, Palmar and Tarsal Human Skin and through Toe Nails.** *Arch. Dermat. & Syph.* 1946, Jan., v. 53. No. 1, 39–41, 3 figs.

LUCKIESH, M., TAYLOR, A. H., COLE, H. N. & SOLLMANN, T. **Protective Skin Coatings for the Prevention of Sunburn.** *J. Amer. Med. Ass.* 1946, Jan. 5, v. 130, No. 1, 1–6.

This is an account of researches undertaken in December 1942 for the U.S. Army Air Force, to provide an "effective protective substance for the prophylaxis of sunburn." It was a collaboration between two physicists, Luckiesh and Taylor, and two physicians, Cole and Sollman. From previous observations on the ultra-violet absorbing power of different substances, it was decided

to concentrate only on preparations and mixtures containing any of the following: titanium dioxide, salicylates, zinc oxide, and petroleum jelly. Various mixtures of two or more of these were tested, including several proprietary preparations; several different varieties of petroleum jelly without anything added were also tried. Physical tests showed almost complete absorption of ultra-violet radiation by 0·03 mm. of a phenyl salicylate and petrolatum flavum mixture, with or without added zinc oxide. Dark red vet. petrolatum was also selectively opaque to the erythemo spectrum. Titanium dioxide was not so effective. For a biological test small areas of skin covered with the material being tested were exposed for varying periods to high intensity radiation, and any development of erythema was noted; without a protective coating on the skin erythema was usually produced with about 15 seconds' exposure. It was found that zinc oxide diminished the protective power of the salicylate petrolatum mixtures: and that the dark red petrolatum gave complete protection for exposures of 20 minutes.

A factor of practical importance was resistance to washing, as the preparation was to be used by aviators who might be brought down into the sea; poor resistance to washing eliminated preparations with a cold cream basis. Resistance to freezing was also necessary as the petrolatum would be carried in aircraft and might thus be frequently frozen: this eliminated mixtures containing water. The final recommendation was that two kits should be tried in practice, and their respective values compared: Kit A, of dark red vet. petrolatum, and Kit B, of dark red petrolatum with 10 per cent. phenyl salicylate. The dark red petrolatum did not produce any irritation when applied daily to the skin of one investigator. [The effect upon sweating of the protective layer on the skin was not considered.] *W. S. S. Ladell.*

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## TROPICAL ULCER.

BRECHER, G. **Ambulatory Treatment of Tropical Ulcers.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 449–54. [10 refs.]

In the southern peninsula of the Republic of Haiti, West Indies, facilities for the treatment of ulcers of the leg in hospital were inadequate, so a routine fo m of ambulatory treatment was adopted, with good results. Yaws is almost universal in that part of Haiti and skin lesions of yaws were present in nearly half the patients treated for ulcer of the leg, but the author concluded that most of the ulcers could be regarded as tropical ulcers.

The routine local treatment used was the one introduced for chronic ulcers of the leg by BAYNTON of Bristol in 1799; heated adhesive strips [material not stated], ½ to 1 in. wide, were applied vertically or obliquely, but not circularly, and slightly overlapping each other, so as to form an occlusive dressing over the ulcer and covering the surrounding skin for 3 ins. above and below and 1 in. at the sides. This was covered by a bandage and the dressing was changed about once a week.

Systemic treatment was also given; neoarsphenamine was injected intravenously and bismuth subsalicylate in oil intramuscularly once a week on the same day.

Of 205 cases so treated, 147 (71 per cent.) were known to have healed, the other 58 having been lost sight of. Of these 147 cases, 51 (35 per cent.) healed in under 30 days, 74 (50 per cent.) in 30–60 days, 10 (7 per cent.) in 60–90 days, and 12 (8 per cent.) in 90–150 days. Of the 58 cases lost sight of, 46 had

improved and 12 were unimproved when last seen. Some complications are mentioned and there were two deaths which the author suspects were due to toxic nephritis caused by arsphenamine in patients with hookworm infestation.

The author thinks that better results would have been obtained if the diet of the patients, which was deficient in higher protein and calcium, could have been improved. *J. F. Corson.*

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## MISCELLANEOUS DISEASES.

POWER, S. **Funiculitis in British Troops in Ceylon.** *Lancet.* 1946, Apr. 20, 572–3.

The author records "an outbreak among the British troops of what, for want of a better name, may be called funiculitis"; it occurred in Ceylon in 1943 after the onset of the south-west monsoon. The disease was characterized by local induration of the spermatic cord due to thrombosis in the veins. Notes of two cases are given. No special treatment was required; if seen at the onset, the patients had a few days' rest in bed, while if first seen later, they were told to wear a suspensory bandage.

The author does not think that it was caused by filariasis, although that would be suggested by its being endemic and seasonably epidemic in Ceylon; the locality was non-filarial, none of the patients showed eosinophilia, no filariae were found in the blood or hydrocele fluid, the "pathology was not of the filarial type," and filariasis is uncommon among Europeans [but see recent records of early filariasis among American troops, abstracted in this *Bulletin*].

[Endemic funiculitis is stated by MANSON-BAHR ("Manson's Trop. Dis.," 1945, 12th ed., London, Cassell, p. 726) to be undoubtedly of filarial origin. It was described in Egypt by MADDEN (*Lancet*, 1907, v. 1, 505) and COUTTS (*Ibid.*, 1909, v. 1, 227); and in Ceylon by CASTELLANI (*ibid.*, 1908, v. 2, 15) who isolated a diplo-streptococcus which he thought was a secondary infection. CASTELLANI and CHALMERS ("Manual of Trop. Med.," 1919, 3rd ed., London, Baillière, Tindall and Cox, p. 1939) regarded it as a filarial condition with a superadded streptococcal infection. STEPHENS and YORKE (see "The Practice of Medicine in the Tropics," by BYAM and ARCHIBALD, 1923, v. 3, 1920) considered it to be due to filariasis. STITT also ("Diagnosis, Prevention and Treatment of Tropical Diseases," 1942, p. 1317) regards it as filarial in origin. It was reported from Kenya by JEWELL (this *Bulletin*, 1925, v. 22, 990) who was convinced that the disease was *sui generis*. CASTELLANI (*ibid.*, 1918, v. 11, 212) saw a case in Macedonia.] *J. F. Corson.*

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## GENERAL PROTOZOOLOGY.

SENEKJIE, H. A. & LEWIS, Ruth A. **An Inquiry into the Growth Factor or Factors of certain Blood and Tissue Flagellates.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 345–8.

The authors have studied the culture requirements of species of *Leishmania* and *Trypanosoma cruzi*, with a view to the discovery of the growth-promoting factor which exists in the blood. It was found that the factor is present in serum but is not directly associated with albumin, euglobulin, pseudoglobulin or combinations of these. It is not present in haemoglobin nor in washed erythrocytes. It is destroyed at a temperature of 100°C., but partially survives

30 minutes' exposure to 70°C. It was shown that para-aminobenzoic acid, pyridoxine, nicotinic acid, thiamin and other vitamins tested, were all unable to take the place of the factor, which is dialysable and is probably lost during the process of fractionating the serum proteins. *C. M. Wenyon.*

WEINMAN, D. **Human Toxoplasma.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Dec., v. 20, No. 2, 125–61, 4 pls. [Refs. in footnotes.] [Spanish version 162–93.]

This is a useful general account of human toxoplasmosis based on published work of the author himself and others who have investigated the disease, particularly in the United States during the past ten years. *C. M. Wenyon.*

DOW, R. S. **Toxoplasmic Encephalitis : Clinical Findings in 2 Patients from Pacific Northwest.** *Northwest Med.* 1945, Dec., v. 44, 382. [Summary taken from *J. Amer. Med. Ass.* 1946, Mar. 23, v. 130, No. 12, 821–2.]

Dow presents the histories of two patients with toxoplasmic encephalitis. The first was a child aged 2 who exhibited all the clinical manifestations of toxoplasmic encephalitis, including (1) healed or inactive chorio-retinitis, (2) reduced vision, (3) strabismus nystagmus and microphthalmos, (4) intracerebral calcification, (5) one convulsive seizure, (6) internal hydrocephalus from a block at the aqueduct of Sylvius, (7) retarded speech development, and (8) mental deficiency. The case was complicated by the presence of a postoperative Staphylococcus aureus meningitis and wound infection. The serologic tests for toxoplasma had not been done, and attempts to infect laboratory animals with spinal fluid were unsuccessful. The second patient, a girl aged 5, exhibited many of the signs and symptoms of toxoplasmic encephalitis. Treatment with sulfapyridine was tried and continued for ten days, maintaining a blood level of 5 to 10 mg. per cent. She seemed much improved for three weeks, but then seizures recurred. This observation and the results obtained in laboratory animals make it desirable to continue the use of sulfonamides whenever a diagnosis of toxoplasmic encephalitis is made and when there has not been extensive permanent cerebral damage. It is felt that the condition is more common than the reported cases would indicate and that a greater incidence will be found when knowledge of this disorder has become more generally available.

COWEN, D. & WOLF, A. **Toxoplasmosis in the Monkey. Acute Fatal Infection experimentally produced in a Young** *Macaca mulatta.* *J. Infect. Dis.* 1945, Sept.–Oct., v. 77, No. 2, 144–57, 11 figs. on 2 pls. [25 refs.]

Earlier attempts to infect monkeys with toxoplasma have given negative results as regards the demonstration of parasites by microscopic examination of tissues. Some evidence was obtained, however, that rhesus monkeys, as determined by inoculation of blood into mice or by serological tests, might acquire a transient infection. In the experiments described in this paper attempts were made to infect, by intracerebral and other methods of inoculation, nine rhesus monkeys of which two were immature animals 7 months of age, two were young adults and three were pregnant females, and two were infants, the offspring of the pregnant animals. In addition a young African green monkey (*Cercopithecus sabaeus*) and an adult baboon (*Papio doguera*) were also injected. Of these animals, one young rhesus monkey succumbed to the infection and showed toxoplasmic focal myositis and lesions in the rete testis. This is the first instance of active toxoplasmosis in a monkey with the production of lesions. Of the other 10 monkeys, four gave a positive result

in serum neutralization tests for toxoplasmosis. Three monkeys, including two of those giving a positive result in serum neutralization tests, had myocardial lesions which were probably due to toxoplasmic infection, though no parasites could be demonstrated in them. The attempt to produce congenital infection by the inoculation of the three pregnant monkeys was unsuccessful. From the experiments described in this paper, which were carried out with a human strain maintained in mice, and from the earlier work, which is reviewed, it is evident that primates are relatively insusceptible to toxoplasmosis.

*C. M. Wenyon.*

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## GENERAL ENTOMOLOGY.

CAMERON, T. W. M. **Insecticides and Repellents in Modern Medicine.** Reprinted from *McGill Med. J.* 1945, Oct., v. 14, No. 3, 14 pp.

This is a brief factual statement of information at present available on the insecticides and repellents now used in medicine, and in it the author describes briefly the composition and effects of pyrethrum, Lethane 384, Lethane 384 Special, Thanite, derris, DDT, DDD (the dichlorethane equivalent of DDT, which has a similar action but is only about one-tenth as toxic to mammals), Gammexane, the oils used as larvicides, Paris green, paradichlorbenzene, orthodichlorbenzene, and sodium arsenite. The repellents mentioned are oil of citronella with pyrethrum concentrate, Indalone, Rutgers 612, dimethyl and dibutyl phthallate, a new repellent NMRI 201 developed in the United States, and benzyl benzoate.

In so short a paper the information given is necessarily compressed, and the outline is brief. Nevertheless, this is a useful summary, which a student of tropical medicine could read with advantage. The author points out that medical entomology saw its modern beginning with the work of Manson, and that it is now the backbone of public health work in the tropics. Information has accumulated so rapidly during the war that there is need of summaries of this kind, to make the subject clear to those who wish to keep abreast of research but who are not actively engaged in it. *Charles Wilcocks.*

DAVID, W. A. L. **Factors influencing the Interaction of Insecticidal Mists and Flying Insects. Part I—The Design of a Spray Testing Chamber and some of its Properties.** *Bull. Entom. Res.* 1946, Feb., v. 36, Pt. 4, 373–93, 4 figs. [12 refs.]

The cabinet described was specifically designed for testing insecticides for use against mosquitoes but it can be used with other flying insects. It is a chamber in which temperature and humidity are controlled, of 54·5 cu. ft. (1,543 litres) internal capacity, into which the spray is atomized by an Aerograph spray gun. The insects are exposed in wire frames covered with paper except for two wire-mesh ends through which the spray can penetrate, and knock-down counts can be made through special windows in the cabinet. These cages can be inserted or extracted without opening the cabinet door.

The author points out that the effects of variation in testing conditions are little understood, and testing of sprays has hitherto been done under arbitrary fixed conditions in order that tests may be repeated. Experiments were therefore planned to investigate various factors.

(i) The activity of the mosquitoes was very important because, when the spray has evaporated down to floating particles (mist), the insecticide is mainly gathered by the insect as it flies through it. Very dilute pyrethrum preparations irritate the insects and stimulate flight, but this does not occur with DDT

sprays. The kill produced by the latter, therefore depends to a large extent on the natural activity of the insects, which varies in different cultures. To overcome this source of variability it is advisable to include a small, non-lethal, concentration of pyrethrins, so as to obtain uniform activity.

(ii) After the spray has been released, the more volatile fraction (kerosene) evaporates rapidly if the dose is below 15 cc. of liquid per 1,000 cu. ft. The chances of a drop of insecticide impinging on an insect are considerably reduced as the diameter falls below 5–10 microns. Therefore, the concentration of non-volatile substance in the spray fluid is important, and it can be shown that *part* of the effect of some synergizing materials (*e.g.* sesame oil, iso-butyl undecyleneamide) is due to the larger drops of spray left when they are present.

(iii) There is a positive correlation between temperature and susceptibility of the mosquito *Aëdes aegypi* to pyrethrum, as shown by results at 20°C. and 30°C.

(iv) The humidity during actual exposure, however, has little influence over normal ranges, judging from results at 40 per cent. and 80 per cent. R.H.

(v) In this cabinet the time of introduction of the insects was investigated. Kill was highest when they were inserted before spraying, and fell gradually to 10 minutes after spraying. The order of effectiveness of several formulae was not altered, however.

(vi) Some tests were made with insects flying freely in the cabinet, to compare with those in cages. The kills were higher in all cases when non-volatile constituents were added to the sprays, but the relative results were similar.

*J. R. Busvine.*

FAIRCHILD, G. B. & BARREDA, E. A. **DDT as a Larvicide against** *Simulium*. *J. Econom. Entom.* 1945, Dec., v. 38, No. 6, 694–9.

The experiments aimed at eradication of *Simulium spp.*, the vectors of *Onchocerca volvulus* in Guatemala and southern Mexico.

Experiments in Guatemala showed that addition of a 4 per cent. DDT emulsion concentrate to streams to give a dilution of one part DDT in ten million, killed *Simulium* larvae for a distance of ten kilometres along the stream.

Attempts to give a prolonged insecticidal action were made by compounding the DDT in blocks of plaster of paris, in sawdust and in Esparto sponge gourds. Effective kills resulted, but lasted only one or two days.

Further tests showed that DDT powder made into a suspension in water, with a wetting agent, gave kills as satisfactory as those obtained with emulsions. It seems possible that this is due to aqueous solution of DDT at a rate of one part in 10 to 15 millions of water. *J. R. Busvine.*

EBELING, W. **DDT Penetration prevented by adding Aluminum Stearate to DDT-Kerosene Solutions.** *J. Econom. Entom.* 1945, Dec., v. 38, No. 6, 689–91, 1 fig.

The addition of 1 per cent. aluminum stearate to kerosene greatly retards its penetration into foliage leaves. The effect when a DDT solution in kerosene (4 per cent.) is used, is to keep the solution on the surface of the leaves so that DDT crystals are left exposed instead of penetrating the plant. The effect is sufficiently great for trees which have been sprayed with DDT solution plus aluminum stearate to be picked out from controls (DDT solution only), by the visible white deposit. *J. R. Busvine.*

HOCKING, K. S. **The Use of "666" in the Control of** *Ornithodoros moubata*, **Murray.** *East African Med. J.* 1946, Feb., v. 23, No. 2, 50–55.

As the tick *O. moubata* normally lives beneath the surface of the soil, it is difficult to eradicate it from infested buildings. "666" (benzene hexachloride, crude material containing 12 per cent. of the active gamma isomer) and DDT were tested in the laboratory and the field against this tick. Although the laboratory tests suggested that the "666" sprayed at a rate of 1,250 mgm. per square foot should give complete control, in native huts it proved less effective, though it substantially reduced the tick population. A second application of "666" three weeks later seemed to eliminate the ticks. DDT also reduced the number of ticks, but was considerably less effective than the "666". *Kenneth Mellanby.*

KEARNS, C. W., INGLE, L. & METCALF, R. L. **A New Chlorinated Hydrocarbon Insecticide.** *J. Econom. Entom.* 1945, Dec., v. 38, No. 6, 661–8.

The compound has the empirical formula $C_{10}H_6Cl_8$ and is referred to as "1068". It is a colourless, odourless, viscous compound boiling at 175°C. It is readily soluble in most organic liquids and is completely miscible with odourless kerosene. The sample examined, which was at least 99 per cent. pure, showed no tendency to irritate skin or mucous membranes.

Insecticidal tests were made against a number of different insects in comparison with pure DDT and *gamma* benzene hexachloride. To the pea aphid (*Macrosiphum pisi*) the colorado beetle (*Leptinotarsa decemlineata*) and the adult squash bug (*Anasa tristis*), 1068 was definitely more toxic than DDT.

As a residual film on wallboard, 1068 was intermediate in speed of knockdown of *Anopheles quadrimaculatus* adults between DDT and benzene hexachloride, the latter being most rapid. The order of efficiency as regards persistence was reversed, DDT being most lasting.

Tests against larvae of *A. quadrimaculatus* indicated that the three substances were of the same order of toxicity.

Peet Grady tests with houseflies (*Musca domestica*) gave median lethal concentrations as follows: DDT, 0·06 per cent. and 1068, 0·02 per cent.

Experiments in which solutions were delivered to the prothorax of individual roaches (*Periplaneta americana*) indicated a toxicity for 1068 three times as great as that of DDT.

Finally, the various compounds were tested as stomach poisons for the grasshopper *Melanoplus differentialis*. The median lethal doses were:—

| | |
|---|---|
| *gamma* benzene hexachloride ... ... | 5–10 micrograms per gram. |
| 1068 ... ... ... ... ... ... | 12–25 ,, ,, ,, |
| DDT ... ... ... ... ... | over 50 ,, ,, ,, |

*J. R. Busvine.*

GRANETT, P. & HAYNES, H. L. **Insect-Repellent Properties of 2-Ethylhexanediol-1, 3.** *J. Econom. Entom.* 1945, Dec., v. 38, No. 6, 671–5.

The compound 2-ethylhexanediol-1,3 has been known during the war as Insect Repellent No. 612, the test number assigned to it at Rutgers University. It is a slightly viscous, colourless liquid having a mild odour resembling that of witch-hazel. It is stable under extremes of storage conditions and, unlike certain other repellents, its solvent action on certain materials is relatively weak. It will not attack cellulose acetate, cellulose nitrate, polystyrene, vinylite resin UYNS, Lucite or Plaskon. The vapour pressure at 20°C. is only 0·01 mm., and it boils at 244°C. and freezes below −40°C. Solubility in water is 4·2 per cent. at 20°C.

In tests in which 1 cc. of material was applied to 100 square inches of skin, the compound compared with dimethyl phthalate as follows :—

| Insect | Time to first bite | |
|---|---|---|
| | 612 | Dimethyl phthalate |
| *Aëdes aegypti* ... ... ... ... ... | 9 hr. | 7–8 hr. |
| *Anopheles quadrimaculatus* ... ... ... | 1 ,, | 2 ,, |
| *Aëdes sollicitans* / *A. cantator* ... ... ... ... | 6 ,, | 4 ,, |
| *Anopheles albimanus* ... ... ... ... | 3–4 ,, | 1½–2 ,, |
| *A. punctulatus farauti*... ... ... ... | 6 ,, | 1 ,, |
| *Stomoxys calcitrans* ... ... ... ... | 1½–2 ,, | 1 ,, |
| *Simulium* spp. ... ... ... ... ... | 6 ,, | 5½ ,, |
| *Phlebotomus* spp. ... ... ... ... | 4 ,, | 4 ,, |
| *Ctenocephalides canis* / *C. felis* ... ... ... | 2 ,, | 4 ,, |
| | on treated suits | |
| *Eutrombicula* spp. / *Acariscus maroni* ... ... ... | 30± days | 30± days |

It will be seen that "612" compares well with dimethyl phthalate, being more effective against all insects except *Anopheles quadrimaculatus* and the fleas. *J. R. Busvine.*

HATOFF, A. **Desensitization to Insect Bites.** *J. Amer. Med. Ass.* 1946, Mar. 30, v. 130, No. 13, 850–54.

"In a series of 129 susceptible infants and children, 4 out of 5 were benefited by the use of flea antigen. This constitutes a demonstration of one method of developing host immunity to insect bites. The importance of this demonstration lies in the possibility of the use of such a method as an adjunct in the control of insect borne diseases."

FREEMAN, R. B. **The Pig as a Host of *Pulex irritans* L. (Siphonaptera, Pulicidae).** Reprinted from *Entomologist's Monthly Magazine.* 1946, Jan. 30, v. 82, 19–21. [10 refs.]

The human flea, *Pulex irritans*, is found on many mammals but most of them, especially rodents, are probably not true hosts, the flea being unable to maintain permanent colonies on them ; some, however, are true hosts, the domestic pig being probably the most important, while the dog is also often infested [see MAC ARTHUR, this *Bulletin*, 1946, v. 43, 602]. The author gives references to reports of the infestation of pigs in Great Britain, the United States of America, Argentina, Australia, and Morocco [this *Bulletin*, 1925, v. 22, 916]. LEWIS (*Gaz. Leckford Estate*, Andover, 1936, v. 1, 104) reported an outbreak on a farm which had been "famous for fleas for the past thirty years or more" ; they became a serious pest after the arrival of pigs on the farm.

A severe infestation of the pigs on a pig farm at Adderbury, Oxfordshire, was investigated in 1938 ; all the farm buildings, the two cottages, and the yards were heavily infested, and the surrounding fields contained considerable populations of the fleas ; "wherever the harmless looking mass of bits of straw and dry loam was disturbed it was seen to be a seething mass of jumping fleas" [quoted by the author from a report]. Since the pigs were removed [apparently in 1940] severe outbreaks of flea infestation were noted, twice in 1942 and once

in 1943 ; " It is certain, however, that these fleas must, in the 1943 case, have survived in some stage or other without a blood meal for three years," which is longer than any laboratory record. The infestation apparently died out as there are no records of it in 1944 and 1945.

Fleas were not found on the pigs and they probably fed when the pigs were lying down. *J. F. Corson.*

RADFORD, C. D. **Notes on *Trombicula deliensis* Walch, 1923 (Acarina ; Trombidiidae), with Description of the Adult.** *Parasitology.* 1946, Jan., v. 37, Nos. 1/2, 42–5, 9 figs.

An account is given of experiments made in an attempt to rear *Trombicula deliensis*, a mite whose larva is believed to be an important vector of scrub typhus (tsutsugamushi disease). It proved impossible to complete the whole life-cycle in the laboratory, but all stages were obtained, nymphs from larvae attached to wild rats, bandicoots and shrews obtained by trapping, and larvae from adults extracted from the soil. The nymphs died soon after moulting ; too few larvae were obtained to continue the cycle. An account of the morphology of the adult, which has not previously been described, is given, with some notes on its biology. *Kenneth Mellanby.*

RADFORD, C. D. **Larval and Nymphal Mites (Acarina ; Trombiculidae) from Ceylon and the Maldive Islands.** *Parasitology.* 1946, Jan., v. 37, Nos. 1/2, 46–54, 29 figs.

Some details of the morphology of the larvae and nymphs (together with the adult of *Neoschöngastia indica*) of several species of Trombiculid mites of possible medical importance are given, with notes on the technique used when attempting to breed them in the laboratory. One new genus of Trombiculidae, *Womersleyia*, and the genotype, *W. minuta*, is described ; as this is parasitic on grasshoppers it is unlikely to be of medical importance.

*Kenneth Mellanby.*

CARTER, H. F. & D'ABRERA, V. St. E. **Mites (Acarina)—a probable Factor in the Aetiology of Spasmodic Bronchitis and Asthma associated with High Eosinophilia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Apr., v. 39, No. 5, 373–87, 1 chart. [23 refs.]

Twenty-five Ceylonese patients, all with a high eosinophilia (over 3,000 per cmm., as against a normal 500 per cmm. for individuals in the tropics) and all but one with bronchial asthma or other respiratory symptoms, were investigated. Treatment was given with organic arsenicals, and 24 out of 25 responded satisfactorily, both as regards clinical symptoms and as to eosinophilia, the latter being greatly reduced within three weeks.

Samples of sputum from these patients were collected with rigorous precautions to prevent contamination. Mites, mostly tarsonemids or tyroglyphids, were recovered from all cases. After treatment with arsenicals the number of mites was strikingly reduced. There is no doubt that these mites came from the lungs.

Most of the mites collected are normally found among food and stored products, and it is suggested that some of these may be able at times to colonize the bronchi. Cases are described in which allied mites have been recovered from human tissues. These creatures are almost ubiquitous in tropical countries, and can live under very diverse conditions, so it is not impossible that they can invade living tissues. In some of the cases described it seems

probable that the mites were really established as parasites in the lungs; in others the mites were probably casual invaders.

The relation between the mites and the symptoms is discussed. A patient sensitized to the mites and their products would be likely to show more acute symptoms with only a few mites in the lungs than an unsensitized individual with a great parasite population. This may account for some apparent discrepancies in the results. The thesis that the mites may be the cause of the asthmatic symptoms and the eosinophilia seems to be well established by this work. [See also the previous paper on the subject, this *Bulletin*, 1945, v. 42, 73.] *Kenneth Mellanby.*

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## LABORATORY PROCEDURES.

BROWN, R. L. **Comparative Studies on Enterozoic Parasite Ova and Cysts Concentrating Procedures.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 375–6.

The author has made a comparison of two techniques for the concentration of protozoal cysts and helminth eggs in faeces. These were the de Rivas acetic-acid-ether method [this *Bulletin*, 1928, v. 25, 447] and the zinc sulphate method. In all cases the methods were applied to an emulsion of the faeces in physiological saline, filtered through two layers of gauze. In the de Rivas method 5 cc. of the filtrate were shaken up with 30 cc. of 5 per cent. acetic acid. The mixture was filtered through gauze, and an equal volume of ether was added. This was shaken until it jellied. It was then centrifuged. Two drops of the deposit were taken up and examined for cysts or ova. In the zinc sulphate method, 5 cc. of the filtrate were diluted with 60 cc. of tap water, and centrifuged. The fluid was poured off, and the deposit taken up with tap water and again centrifuged. This process was repeated till the supernatant fluid remained clear. The sediment was then taken up in zinc sulphate solution of specific gravity 1·180, and again centrifuged. Two drops of the surface film were then pipetted off for examination. It was found that, generally, the zinc sulphate technique proved to be the more reliable, though it occupied more time than the de Rivas method, which in the case of some cysts and ova failed to concentrate at all. Furthermore, the de Rivas method produced more distortion. For routine examinations the zinc sulphate method is to be preferred as it was much less selective, concentrating more nearly uniformly all cysts and ova, with a minimum of distortion. *C. M. Wenyon.*

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## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

NAPIER, L. E. **Teaching of Tropical Medicine.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Feb., v. 39, No. 4, 273–82. Discussion pp. 283–300 [MANSON-BAHR, P.; GORDON, R. M.; MACDONALD, G.; HODGE, E. H. V.; DREW, W. R. M.; STANNUS, H. S.; TROWELL, H. C.; CHRISTOPHERS, R.; NAPIER, L. E. (in reply); SHORTT, H. E.].

Dr. Napier began his address by stating that Great Britain was rapidly losing any lead which it may have had in the field of tropical medicine, and that the subject appeared to have been relegated to the place of a specialization about which the general practitioner need know nothing, and with which the ordinary undergraduate student should not be burdened. This unfortunate attitude was exemplified in the *Goodenough Report*, where the existence of

parasites other than bacteria was apparently not recognized, and in which there was no suggestion that the undergraduate student need be introduced to diseases which were not prevalent in his own country ; moreover, under the heading of postgraduate teaching, clinical tropical medicine was dismissed as a subject that could not possibly be taught in Britain. The speaker emphasized the fallacy of segregating so-called " tropical medicine " ; of teaching parasitology to the student, with bacteria as the only examples of parasites ; and, while in his later years, of teaching him virtually nothing of the pathology, symptomatology and therapeutics of tropical diseases.

Dr. Napier next discussed how this unfortunate state of affairs might best be remedied. In the undergraduate years it was of importance to avoid further overloading of the curriculum, but much might be done by introducing the student during his pre-medical years to the pathogenic micro-organisms and worms, and by substituting, both in name and scope, parasitology for bacteriology. If this system were adopted it would leave the pathology, symptomatology and therapeutics of important tropical diseases (many of which presented excellent opportunities for the teaching of the general principles of preventive medicine) to be taught in the systematic lectures on medicine in the wards and out-patient departments when the occasion arose. Such teaching would necessitate a generous supply of material for the practical classes in parasitology, and for the teaching of clinical pathology and histology ; clinical material would have to be made available for the later years. In the United States this difficulty was faced and overcome very early in the war by the co-operation of the Army Medical School at Washington, which distributed suitable material to all the medical schools in the country. Later, some of the schools, through their tropical connexions, contributed to the common pool, and the organization is at present receiving an abundance of material from the thousands of postgraduate students now serving in various tropical fields. The importance of clinical material is obvious, and a considerable amount of such material is now available in Britain, although it is sometimes " missed ". Dr. Napier considered that during the next few years there would be an increasing number of cases of tropical diseases among the personnel of the fighting forces and among civilians whom the war has taken into the tropics. Even in the absence of such cases, however, much could be done with the aid of a good set of lantern slides, preferably in colour, or better still with cinema films.

As regards postgraduate teaching, Dr. Napier thought that it would be a tragedy, with considerable political and financial as well as medical repercussions, if we were to allow America or any other country to take the lead in the postgraduate teaching of tropical medicine, and to attract to their country doctors and even patients from India and the Dominions, the Colonies, and foreign countries, who would otherwise have come to London or Liverpool. In London there was an abundance of clinical material, which would show a marked increase during the succeeding years, but at present no hospital where it could be collected. The most crying need to-day was a " tropical medical centre " where all such persons returning from the tropics could go for diagnosis and treatment. There was a popular misconception that, in medical practice in any tropical country, one would encounter a very large variety of the diseases usually labelled " tropical ". Actually there were few, if any, places in the world where one could see a better selection of tropical diseases than in London. The object of a post-graduate course in tropical medicine should be, not to make the student an expert in all tropical diseases, but to give him additional knowledge to enable him to take advantage of the opportunities to become an expert, which would be provided in his subsequent practical experience in whatever tropical centres he might visit. The speaker seriously questioned the value of instituting a higher diploma, of specialist status, in tropical medicine

but, if any teaching body wished to institute such a degree, then they should demand several years' experience under approved supervision in two or more tropical centres. Dr. Napier stated that he did not propose to discuss the syllabus for an adequate postgraduate course in tropical medicine, but he showed a scheme which he had drawn up for a School of Tropical Medicine in the United States and which had formed the subject of a paper read by him at the Annual Meeting of the American Society of Tropical Medicine [see this *Bulletin*, 1946, v. 43, 77].

In conclusion Dr. Napier made two proposals : (1) That the Royal Society of Tropical Medicine and Hygiene should prepare a memorandum on the teaching of " tropical medicine " to the undergraduate student, and should circulate it to universities, medical schools, examining bodies, and others likely to be interested, in Great Britain and Ireland, and possibly in the Dominions, Colonies, and India ; (2) that it should endeavour to obtain direct representation on all committees concerned with policy in the teaching of " tropical medicine ", both undergraduate and postgraduate, or with research in tropical diseases, which, of course, will include committees concerned with any tropical diseases hospital.

In the discussion following this paper Sir Philip MANSON-BAHR emphasized the danger of overburdening " that much abused poor creature—the medical student—" with additional studies, but supported the view that much good would result from a study of the human parasitic infections as zoological types during the pre-medical studies. In the clinical years tropical medicine must be taught by a well-grounded physician, who must know the ordinary diseases and keep himself familiar with the trend of ordinary medicine. Professor GORDON, while agreeing with the principles expressed by Dr. Napier, disagreed with him in two important points. In the first place he considered that Dr. Napier's suggestion considerably to extend the subject matter for the D.T.M. & H. would be a mistake. Contrary to the view expressed in the *Goodenough Report*, this diploma did not represent a specialist qualification ; on the contrary, it was intended solely as a rectification, in a period of some 4 or 5 months, of the essential deficiencies in the general medical curriculum prior to qualification. In the second place he disagreed with Dr. Napier's suggestion that a single great tropical medicine centre should be formed in London, where all sick persons returning from the tropics should go for diagnosis and treatment. Professor Gordon thought it fundamentally unsound to focus all the resources, financial and otherwise, in a single institution ; the course of tropical medicine in Britain would best be served if all available resources were directed towards the support and sustenance of the various existing organizations, and not solely to the furtherance of one single project.

Dr. George MACDONALD noted that three proposals had been made for the replacement of the facilities for teaching tropical medicine lost to London as a result of the war. Brigadier Hamilton Fairley had recommended an " Imperial " hospital in association with the London School of Hygiene and Tropical Medicine and the Wellcome Research Institution. Dr. Wenyon had recommended the foundation of a totally new school, or at any rate the divorce of the present School of Tropical Medicine from the School of Hygiene, and its re-establishment around a new hospital. Finally, Dr. Napier had advocated the function of a Tropical Centre similar to that proposed by Hamilton Fairley, but associated with a general hospital. Dr. Macdonald believed that divorce, as suggested by Dr. Wenyon, was not justified, but extension in the form of additional facilities for clinical and chemotherapeutic research should be considered in association with a new hospital. Brigadier Hamilton Fairley's " Imperial " project suggested some exclusive foundation, relegating other

centres to a secondary rank. Certainly Liverpool would have grounds on which to oppose such a proposal, and it was likely that the Dominions would also oppose it, unless they were given an active share in its initiation and subsequent running. Dr. Macdonald suggested the formation by the Society, of a Policy Committee which would, firstly, examine and erase the divergencies of opinion about the best method of developing and maintaining, in London and elsewhere, British pre-eminence in tropical research, and secondly, agree on, and press for acceptance of, standards of teaching and examination for both general practitioners and specialists in medicine and hygiene. Lieut.-Colonel E. H. Vere HODGE agreed with previous speakers in supporting Dr. Napier's main contentions and in paying tribute to the excellence of its presentation. He thought that it was neither feasible nor desirable to direct all sufferers from tropical disease to one institution, and that it would be necessary to maintain tropical diseases units, with experienced staffs, attached to general hospitals throughout the country. His experience before and during the war had led him to the conclusion that teaching activities should not be solely conducted with a view to the diploma. These activities should be of three types : first, undergraduate training, along the lines suggested by Dr. Napier ; second, a three months' course for the benefit of those proceeding abroad for the first time ; third, the course for the diploma, which should be divided into two parts, the second of which could be taken only by candidates who had done at least one tour of service abroad. Lieut.-Colonel W. R. M. DREW gave an account of the teaching of tropical medicine to Army and Air Force officers during the war. He endorsed the suggestion of previous speakers that the Society should take an active part in formulating a definite policy for the teaching of tropical medicine. Dr. H. S. STANNUS believed that the time had passed for attempting to teach the medicine of tropical countries in Great Britain. He envisaged the establishment of medical centres in various parts of the world where medical officers, who had completed a shortened and simplified course at the tropical medical schools in Britain, might spend six months as house-officers in both European and Native hospitals. At each of these centres would be established complete up-to-date hospitals both for Europeans and for Natives, with clinical and research laboratories, library and class rooms, and residential college, the whole organization to be under the supervision of a director and staff. Such a centre would not only train the newly qualified medical officer, but would allow district medical officers an opportunity of returning to the centre to carry out research on any problem requiring investigation. Dr. H. C. TROWELL was in profound disagreement with the suggestion that the British undergraduate should be given more detailed knowledge of tropical medicine ; he should be taught principles, not detailed practice. He supported Dr. Stannus's suggestion that, after a brief introduction at home, the student should go to the tropics to pick up his further instruction. Sir Rickard CHRISTOPHERS strongly supported the proposal by Brigadier Hamilton Fairley that there should be a combined School and Hospital of Tropical Medicine in London. This did not mean that such a centre would exclude Liverpool or other centres, but it was incredible that such an institute should not function in the capital of the country. Colonel SHORTT, in a contribution submitted after the meeting, believed that the first essential in attaining the objects advocated by the various speakers was the provision of a Tropical Diseases Hospital worthy of the capital of the British Empire, and he stressed the absolute necessity for the immediate provision of tropical diseases centres working in close collaboration with the present schools of tropical medicine. Such a scheme should be the immediate concern of a small *ad hoc* body representing the Colonial Office, the Dominions Office, the India Office, and the three institutions at present concerned with the teaching of tropical medicine.

[The reviewer has endeavoured to summarize, in as representative a manner as possible, the views expressed by Dr. Napier, and the subsequent speakers at a meeting which he regards as one of the most important in the history of the Royal Society of Tropical Medicine and Hygiene. It should be clear from these summaries that whereas all the members of the Society were in virtual agreement regarding a relatively minor point, the necessity and nature of further instruction in the undergraduate years, they differed widely, not only in regard to the form which postgraduate training should take, but also concerning the much more important and controversial subject of the establishment and maintenance of proposed and existing centres for the treatment and study of tropical diseases, and the teaching of tropical medicine and hygiene. Such differences of opinion are a sign of a healthy society, but if Britain is to maintain its lead in tropical medicine, it is high time that these differences of opinion were the subject of full and frank discussion by representatives, not only of the Society, but of all bodies interested in the control of tropical diseases, and that the conclusions reached should be implemented by the British Government.]

*R. M. Gordon.*

MANSON-BAHR, P. **Tropical Medicine in the British Empire. The Present Position in London.** *Nature.* 1946, Mar. 16, 323–6. [13 refs.]

In this paper Sir Philip Manson-Bahr recalls briefly the history of the development of British research into the problems of tropical medicine, and of the teaching and hospital facilities which have been devoted to that subject in London. The position as regards clinical teaching is now not satisfactory, and this essay is in part a plea for the institution of a centre for teaching and research in clinical tropical medicine adequate to the needs of London.

In the second section of the paper the author reviews some of the discoveries and achievements which have been made during the war, in relation to tropical medicine, the chief emphasis being placed on the suppressive use of mepacrine; the experiments conducted by the team working under FAIRLEY in Australia, are referred to at some length. The use of penicillin is also reviewed.

The final section relates to the prevention of insect-borne diseases by DDT.

[The potentialities of these advances are very great; much of the progress achieved was made under the compulsion of war, when the problems raised were intense and urgent, and when their solution meant the difference between success and failure of whole campaigns. In peace time the urgency is not thought to be so great, and the facilities for fundamental research are, in some ways, not so easily obtained as in war, but medicine is still faced with a multitude of problems, particularly in relation to the health of primitive peoples. To approach the solution of those problems, it is necessary that research and teaching be pursued on a large scale; for the former, very considerable preparations have already been made by the Government, and it is rather for teaching that the author makes his appeal.]

*Charles Wilcocks.*

BOYD, M. F. **International Appraisal of Research in Tropical Medicine. Presidential Address, 1945, American Academy of Tropical Medicine.** *Amer. J. Trop. Med.* 1946, Jan., v. 26, No. 1, 1–4.

## BOOK REVIEWS.

ROGERS, Leonard [K.C.S.I., C.I.E., M.D., F.R.C.P., F.R.C.S., F.R.S., I.M.S. (retd.), etc.] & MUIR, Ernest [C.I.E., M.D., F.R.C.S. Edinburgh, Medical Secretary, British Empire Leprosy Relief Association, etc.]. **Leprosy.** 3rd Edition. pp. xii+280, 88 figs. (78 on 31 pls. & 2 maps). 1946. Bristol: John Wright & Sons Ltd. London: Simpkin Marshall Ltd. [25*s*.]

Rogers and Muir's "Leprosy" is one of the very small number of medical books for which no substitute is available. It is, therefore, fortunate that the authors and publishers have taken such prompt action to prepare a new and better edition, which more than compensates for the loss in the bombing of Bristol of a large part of the remaining stock of the second edition. There is little to add to the comments made in the reviews of the previous editions in this *Bulletin* (1925, v. 22, 256, and 1940, v. 37, 603).

Although research in leprosy has been somewhat restricted during the past six years, some important advances in knowledge have been incorporated in the sections dealing with prophylaxis, aetiology, and the clinical aspects of the disease. Special mention may be made of, modern developments in connexion with the lepromin test, fresh views on the relationship between the two main types of the disease, and the production of new remedies. An observer so cautious and experienced as Dr. Muir has obtained promising results from "diasone" and "promin" in the treatment of certain types of leprosy.

In spite of the destruction by bombing of most of the original blocks, the present edition is even better illustrated than its predecessor; the number of illustrations has been increased to 88, of which 75 are exceptionally clear reproductions, on art paper, of photographs illustrating all the more important skin lesions.

Although the book is intended primarily for medical men and others engaged in dealing with leprosy, research workers will welcome the newly added bibliography, which runs to six pages of lists of books, reports and articles; a special indication is given to show which of the papers contain full bibliographies of special aspects of the disease.

The first half of the volume is by Sir Leonard Rogers, who is universally recognized as the originator and promoter of the modern outlook on the treatment and prevention of leprosy; it deals with the history, epidemiology and prophylaxis of the disease in so vivid a manner that this part of the book will be found intensely interesting as well as profitable, not only by medical men but also by every layman who is concerned with the welfare of the people of affected countries.

The second half is by Dr. Muir, who presents in clear and simple language the fruits of his unrivalled experience of the clinical aspects of the disease and of the practical application of control measures in many countries of the world.

It should again be emphasized that no exaggerated claims are made for the special drugs used in treatment; on the contrary, great stress is laid on the importance of general measures for reinforcing bodily resistance to the infecting organism.

A striking feature of the book is the admirable manner in which the authors have succeeded in catering for the needs of beginners, as well as of experienced workers in the leprosy field. *John W. D. Megaw.*

ALLEN, Glover M. **A Checklist of African Mammals.** *Bulletin of the Museum of Comparative Zoology at Harvard College.* Vol. 83. 763 pp. 1939. Feb. Cambridge, Mass., U.S.A. Printed for the Museum.

In the preface the author states that the mammalian fauna of Africa is now fairly well known but much revision will still be needed as collections in the

larger museums increase. The present book, volume 83 of the Bulletin published by the Museum of Comparative Zoology at Harvard College, gives a classified list of the names of all known African mammals and of all synonyms up to July, 1938 ; the English names of families and genera are also given. The locality where each species indicated by its name or synonym was first found is shown, as well as the geographical range of the species. Such a list is invaluable for reference and for accurate recording of field and laboratory investigations of the epidemiology of many tropical diseases. Information about this publication can be obtained from the Director of the Museum of Comparative Zoology, Cambridge, Massachusetts, U.S.A. *J. F. Corson.*

RICHARDSON, D. T. [Major-General, R.A.M.C., M.C., M.B., Ch.B., D.P.H.]. **British Red Cross Society Tropical Hygiene Manual No. 10.** 2nd Edition. Revised, with Additions by Sir H. Harold Scott, K.C.M.G., M.D., F.R.C.P., D.P.H., D.T.M. & H., F.R.S.E., President, Royal Society of Tropical Medicine and Hygiene, Late Director, Bureau of Hygiene and Tropical Diseases. pp. x+246, 51 figs., 1 map & 6 pls. 1946, London, Toronto, Melbourne & Sydney : Cassell & Co., Ltd.

The first edition of this Manual was published in 1931 ; since that time there have been many advances in the knowledge of tropical diseases, and in the present edition much new matter has therefore been added. The object of the Manual is " to provide a few elementary rules of health for those proceeding to the Tropics for the first time," and it has been written for the layman. There are 13 chapters, which deal with : Climate and Environment, the Problem of Keeping Cool, Diet, Water and other Beverages, Disposal of Waste Products, Tropical Diseases (5 chapters), Worm Diseases, Snake Bite, and Nursing in the Tropics (by Miss M. E. Tippetts, R.R.C.). In an Appendix are given certain useful formulae and other small items of general information, and there is a syllabus for six lectures on tropical hygiene. The present edition has been revised, and largely rewritten, by Sir Harold Scott who, until a few years ago, was Director of the Bureau of Hygiene and Tropical Diseases.

It is always difficult for a medical man to know how far to go in presenting medical information to laymen ; the two dangers of over-elaboration and over-simplification are very real. On the one hand the reader may become fogged in a mass of detail, which, though readily understood by the medical man who knows his basic facts, may seem to the medically untrained person no more than a collection of empirical statements ; on the other hand, over-simplification may repel the intelligent reader. In his revision, Sir Harold Scott has been at pains to give such explanations as are desirable for a reasonable understanding of the subject, and to include such detail as will be useful to the reader, and there are few important points which have escaped mention. In many small books of this kind there is evidence of hasty and careless writing, and of the inordinate riding of personal hobby-horses ; the present book cannot be criticized on these lines, and throughout there is ample evidence of care for the virtues of precision and clarity of expression.

The subject, of course, is tropical hygiene, and the emphasis is therefore on prevention ; the reader should not expect a treatise on the clinical features of the diseases concerned, though some such information is essential to proper understanding of the points made. Emphasis is therefore rightly laid on aetiology, transmission and prevention, and the reader will find not only that he has the opportunity of learning a good deal of what it is all about, but also that he can use the book as a work of reference to which he can turn for answers to a very large number of questions which, from time to time, will demand his attention.

A few points call for comment. On p. 157 reference is made to the value of quinine, taken regularly, for the prevention of malaria ; mention of mepacrine for this purpose has been omitted because the book is for laymen, and the author (H.H.S.) holds the view that mepacrine should be taken only under medical supervision. On p. 153 the reader is advised to make collections of water unattractive to mosquitoes (if drainage is impossible) by cutting down all vegetation in the immediate neighbourhood. It might have been wise to add that certain species of anophelines, some of which are dangerous vectors, breed most freely in water exposed to the sun ; that the judicious use of natural shade is a recognized measure of prevention in certain circumstances ; and that, whenever possible, expert local advice should be sought.

On p. 72, in the section on camping, the author remarks that " eggs and chickens are the only articles of food that should be obtained locally," but surely vegetables which will be cooked, and fruit such as oranges or bananas, which are protected by thick skins, are harmless and necessary. In Africa, meat, milk, fish and other potentially dangerous foods can, very often, be obtained only from uncontrolled local sources ; if thoroughly cooked these can be rendered harmless, and the alternative, to do without them, is not attractive.

On p. 155 the fish *Lebistes reticulatus* is incorrectly spelled *Ledistis*—the only error of this kind found in the book.

Finally, the reviewer feels constrained to ride his own hobby-horse, and protest against the use of the cholera belt, here once more advocated.

Most of these criticisms are unimportant, and from that fact an estimate of the value of this little book ($5\frac{1}{2} \times 4\frac{1}{4}$ ins.) may be made. It has long been difficult to know what book to recommend to people going to live in the tropics, but that is not now the case ; revision of this Manual has been so well and conscientiously done that it can be recommended without reserve to administrative officers, missionaries, traders and others who should know how to protect themselves in hot countries. *Charles Wilcocks.*

Ash, J. E. [Colonel, M.C., U.S.A., Director, Army Institute of Pathology, Army Medical Museum] & Spitz, Sophie [M.D., C.S., A.U.S., Pathologist, Army Institute of Pathology, Army Medical Museum]. **Pathology of Tropical Diseases. An Atlas.** pp. x+350, 941 illustrations on 257 pls. (15 in colour). 1945. Philadelphia & London : W. B. Saunders Co. [40s.]

This book has been compiled by the Director and Pathologist for Tropical Diseases of the U.S. Army Institute of Pathology. In the introduction the authors point out the relatively meagre attention received by the pathological aspects of tropical diseases in most current writings. They have attempted to fill this " void " by the production of an atlas which is designed to be a comprehensive survey of the pathology of tropical disease, with special reference to diseases which were of greatest military importance in the recent war.

The book is divided into clearly marked sections, each comprising a short account of the epidemiology, clinical features, and pathology of the diseases discussed. In each section the text is accompanied by well arranged and beautifully printed photographs and photomicrographs, together with occasional charts and diagrams. Small lists of important references are appended to each section.

The text is clear and precise, and in many diseases well up to date. Its errors lie chiefly in omission. The feature of the book is the illustrations, which are generally excellent. The same cannot be said for some of the accompanying legends, however. For instance, in the section on Filariasis, there is a photograph showing enlargement of the epididymis following bancroftial filariasis ; the

legend beneath this reads " . . . Enlargement of the scrotum (epididymis) is shown."

The section on dysentery is one of the best in the book. Bacillary, amoebic, and balantidial dysentery are discussed in turn, each disease being illustrated by photographs of both morbid anatomical and histological material arranged to show the pathological processes underlying each disease. The complications of amoebic dysentery are set out in the form of a diagram. The section is completed by a group of photographs which illustrate some of the conditions which may be confused with bacillary or amoebic dysentery, including tuberculosis of the gut, typhoid fever and ulcerative colitis. A small section on stool smears in dysentery is added.

There is a good account of the pathology of malaria, accompanied by illustrations which are admirable, with the exception of the coloured photomicrographs, which are hazy and lacking in detail.

One of the most interesting sections is that devoted to filariasis, which is accompanied by 20 pages of photographs and diagrams, including a particularly clear one illustrating the differential diagnosis of the microfilariae.

The illustrations alone make this a book that should be found in every tropical medical library. *B. G. Maegraith.*

TALICE, Rodolfo, V. [Profesor de la Facultad de Medicina de Montevideo (Uruguay), Jefe de Sección del Instituto de Higiene]. **Enfermedades parasitarias del hombre y parásitos de interés médico. Etiologia - Epidemiologia - Patologia - Clinica - Diagnóstico - Tratamiento - Profilaxis.** [Parasitic Diseases of Man, and Parasites of Medical Interest.] Vol. 1, pp. xx+778, 189 figs., including 3 coloured pls. 1944. Editorial Científica del Sindicato Médico del Uruguay.

This is the first volume of a treatise on parasitic diseases and was printed at the end of 1943; we are not told how many volumes there are to be. The preface states that the book is intended for the practitioner and hygienist. Unlike so many other books dealing with parasites, in which too much attention is given to detailed descriptions of the parasites and too little to the diseases, this book attempts to do justice to both, so that it will be useful to the ordinary medical practitioner. It is intended primarily for S. America, as evidenced by the fact that 5 pages only are given to African trypanosomiasis, and 170 to that of S. America.

Volume 1 is devoted to a consideration of the intestinal protozoa, leishmaniasis, trypanosomiasis and spirochaetosis, including rat-bite fever, syphilis and yaws, etc. Under these headings, dealt with from the South American point of view, a vast amount of information is given, somewhat uncritically, most of it being quotations from the literature.

There are three coloured plates, one fairly good showing intestinal protozoal cysts in iodine, a second giving the appearance of *Trypanosoma cruzi* in Giemsa-stained thick films, and a third and somewhat striking one of the appearance of an opened-up guineapig illustrating the jaundice and haemorrhage of Weil's disease. There are about 180 figures in black and white. These are poor and in some cases so bad that they fail to illustrate what is intended.

*C. M. Wenyon.*

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